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ALFRED NOBEL*

BY

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The annual awards of the Nobel Prizes for outstanding achievements in physics, chemistry, medicine, and literature as well as the Peace Prize continually remind us of Alfred Nobel. The splendour and the solemnity of the occasions when the prizes are presented to the laureates in Stockholm and in Oslo in the presence of the Royal Family remind us of the European culture of the late nineteenth century, based as it was on considerable prosperity or, in some instances, on really outstanding wealth. In these darkest days of the year, around December 10, the day of Alfred Nobel's death, when nobody would like to go to Stockholm, except possibly to get a Nobel Prize, the capital of Sweden is the centre for the biggest scientific and literary event of the year. All the civilized world is for a moment paying attention to the Nobel Prizes and to their founder.

I will come back to the Nobel Prizes at the end of my lecture, but now I will take you directly from the enlightened splendour of the Concert Hall in Stockholm to the most God-forsaken place on the British Islands, the sandhills at Ardeer, near Ardrossan, on the banks of the Firth of Clyde in Scotland, where Alfred Nobel in 1871 got the Government's permission to erect a nitroglycerin and dynamite factory in co-operation with a group of Scottish financiers in Glasgow.

"If I had not got my work here," said Alfred Nobel, "Ardeer would certainly be the most depressing place in the world. Picture to yourself everlasting dunes with no buildings. Only the rabbits find a little nourishment here; they eat a substance which quite unjustifiably goes by the name of grass, and of which some few traces are to be found here and there. This is a wonderful sand desert, where the wind always blows, and often howls, filling the ears with sand which also drifts about the room like a fine drizzle. There lies the factory, and most of the buildings have hidden themselves behind sandhills. A few yards away the ocean begins, and between us and America there is nothing but water. Now you will have some idea of the place where I am living; as I have said, without work it would be intolerable."

The factory at Ardeer can be taken as a symbol for Alfred Nobel's creations. It, like his other enterprises, became very successful with time, but in the beginning the same hard wind as in Ardeer was blowing against the young man, sometimes with a terrible strength. There was in fact no wealth to begin with, not even a name.

*Inaugural address to the Postgraduate Medical School of the University of St. Andrews, delivered on October 9, 1958.

The name Nobel is not derived from the Latin word *nobilis*, but from a place named Nöbbelöv, in the South Swedish province of Scania. One of Alfred Nobel's ancestors, Petrus Olofsson, born 1655 in Nöbbelöv, went as a young man to study in the Swedish university town of Upsala. Having been entered in the university register under the name of Petrus Olai Nobelius, the ambitious young man fulfilled his education in law and married a daughter of the famous university chancellor Olof Rudbeck senior, who in his younger days (1653) had discovered the lymph vessels and the thoracic duct simultaneously with Bartholini.

The Nobel Family

The family, though introduced into influential circles and endowed with good hereditary genes, never became prosperous. At the time when Alfred Nobel was born, his father went bankrupt.

Nobel's father, Immanuel Nobel junior, was an inventor of genius with a quite unusual vitality. Between 14 and 17 years of age he sailed as a cabin boy in the Mediterranean with a ship from his hometown, Gäfle, an extremely hard experience for the young boy. The captain and half the crew died at sea. After receiving an incomplete technological education in Stockholm, he established himself as a building constructor, contractor, and inventor. Very soon, however, he started building beyond his means and also had a large part of his work destroyed by fire. In 1833 he went bankrupt. In order to avoid imprisonment and the insistent demands of his creditors, he moved in 1837 to Finland, then under Russian rule, and soon to Russia, where he established himself as a mechanical engineer in St. Petersburg. His wife joined him there five years later together with their two youngest sons, Ludwig aged 11 and Alfred aged 9.

In his workshop in St. Petersburg, Immanuel Nobel made wagon-wheels, steam-hammers, and other tools, but his chief interests soon became explosive mines, based on his own invention, using chlorate and sulphuric acid as a detonator. After Schönbein's discovery of nitrocellulose in 1846 the mines were mostly iron shells filled with this material. Immanuel's mines apparently were square boxes, filled with powder, with long iron poles sticking out from their sides. These poles, when hit by a ship, broke a glass tube with sulphuric acid inside chlorate, sulphur, and sugar, causing a small explosion which lit a fuse, and this in turn set off the powder. It was this idea, of causing a big explosion

by means of a little one, that was to be decisive in Alfred Nobel's life.

When the Crimean War was imminent the Russian Government supplied Nobel with a subsidy for the extension of his factory, and when the war broke out in 1854 the Russian High Command entrusted the mine-laying programme to Nobel. Kronstadt, the fortress Sveaborg in Finland, and the harbour of Reval in Estonia were protected with mines.

Nobel's submarine mines aroused great interest. On the second expedition of the combined Anglo-French fleet to the Baltic in 1855 the British flagship, the steamer *Duke of Wellington*, captured one of the mines. It exploded on deck and killed one man. The Britons had also seen a Russian steamer being badly damaged when running upon a mine. Rumours of the mines and the knowledge of the strong Russian defence forces on shore then prevented the British fleet from sailing into the innermost parts of the Gulf of Finland. Nobel's mines thus contributed to protect Kronstadt from a bombardment of the kind the fleet on their first expedition in June, 1854, had applied so successfully in destroying the Russian fortress at Bomarsund, on the Åland islands in the Baltic.

Immanuel Nobel had thus rendered the Russian Government very great services, and, although a foreigner, was awarded an Imperial gold medal.

But Russia is Russia. The Crimean War ended with defeat. The old Tsar Nicolaus I had passed away. The new Government disregarded the promises made by its predecessor and placed no orders of any kind in Nobel's enterprises, but, to the contrary, supported his competitors. As a consequence Nobel's workshop went bankrupt. This was in 1859. It was a terrible blow for Immanuel Nobel. Broken down and disappointed, he returned in the same year to Stockholm.

Immanuel Nobel was a genius. Only a genius can without any education in chemistry and with only a few years' technical training construct explosive mines and build steam-engines on a large scale in a foreign country. In his later years, broken by bankruptcy and struck by hemiplegia, he still made suggestions for new inventions. Famous is his prediction of the possibilities of the present-day plywood industry. His predictions have all been amply fulfilled, except in one respect. He suggested that coffins should be so built that one who only seemed dead could himself raise the lid, which should be supplied with air holes for breathing and a cord attached to a bell.

Immanuel Nobel's wife, Andrietta, a vigorous and intelligent woman, had the common sense and sweet temper necessary to hold together the marriage with a man like him. It was certainly no pleasant time when, for five years, she was left alone in Stockholm with their three children, and not much better when after that time she had to leave friends and relatives and embark for Russia. She retained her pleasant disposition all her life, however, and was greatly loved by her sons. Until her death in 1889 they used, if possible, to meet in Stockholm every year for her birthday on September 30.

Alfred Nobel was born in 1833, at the time of his father's first bankruptcy. His only formal education consisted of three terms at the elementary school of Jacob's parish in Stockholm at the age of 8 and some instruction in Russia by a private teacher. The education ended when Alfred was 16 years of age. He then had an opportunity of visiting the United States for a short period and of travelling in Europe for a couple of years, partly in order to improve his health.

Through his father, Alfred had been introduced into the field of explosives, and he found many important problems awaiting solution. One of them was the employment of nitroglycerin as an explosive.

Nitroglycerin

An Italian, Sobrero, a pupil of Pelouze's, prepared in 1847 nitroglycerin, "piroglycerina."

Owing to the high risk of explosion, this new compound was very difficult to handle. On the one hand it burnt like an oil without explosion when directly ignited, and on the other could explode at any time during storage or if handled carelessly, particularly if the product was deficiently purified and still contained nitric and nitrous acids. Thus nitroglycerin remained a taboo for technicians for 18 years after its invention. Alfred Nobel succeeded in getting the fluid to detonate at will and to exploit its power.

During the Crimean War a Russian chemist, Zinin, had called the attention of Immanuel Nobel and his son to the possibility of using nitroglycerin in his mines. No practical results came out of the discussion. After his return to Sweden Immanuel tried in 1863 to mix ordinary gunpowder with 10% nitroglycerin, but no real improvement was achieved. Alfred was more successful.

In Russia he had in 1862 placed nitroglycerin in a firmly stoppered glass tube inside a metal tube filled with black powder and ignited the latter by means of a fuse. The whole was thrown into a canal and caused a heavy underwater explosion.

Nobel's Detonator

In 1863 he went to Stockholm to join his father in the work with nitroglycerin. Here Alfred repeated his experiments from Russia, but put the components in reverse order.

Instead of putting a tube of nitroglycerin into a larger tube filled with gunpowder he dipped a small tube of gunpowder, with a fuse attached to it, into a large tube of nitroglycerin. This gave excellent results. On igniting the black powder by means of the fuse, the nitroglycerin exploded, developing its full blasting power.

Nobel's "Patent Detonator" was discovered—Alfred Nobel's greatest invention, which revolutionized the whole technique of explosives and was the most important contribution to the subsequent development of the high explosive industry.

The detonator itself was a very simple piece, a small wooden cylinder about two inches (5 cm.) long containing a tightly sealed charge of ordinary gunpowder and with a fuse attached to it. New and more efficient detonators like fulminate of mercury were later found, but the principle remained the same. This is considered to be the greatest invention of its kind after the invention of the black powder.

In 1864 he received the Swedish patent for the manufacture and use of nitroglycerin and organized in the same year a small laboratory for the production of pyroglycerin at Heleneborg, in Stockholm.

The interest in the new blasting technique was tremendous. The State Railways and different mining companies soon realized the possibilities presented by Nobel's patented blasting oil, and began using it immediately.

During the following years Alfred Nobel was occupied by acquiring patents in different countries and setting up factories, by no means an easy task.

Nitroglycerin Explosions

Manufacture of the explosive was not free from risk. The first serious accident occurred in Sweden in 1864, when Nobel's Heleneborg laboratory in Stockholm blew up on September 3. On this occasion Alfred's youngest brother, Emil, was killed.

A Hamburg paper of December 4, 1865, contained a comprehensive description of such an explosion which happened in New York. In a small hotel in Greenwich Street a German traveller had left a demijohn carefully wrapped in a box, containing 10 lb. of nitroglycerin, which he said he would fetch later. The box was left with the porter and was used alternatively as a seat and as a foot-rest in boot-polishing. One Sunday morning a waiter noticed that red fumes were issuing from it. The porter carried it out into the street and returned to the hotel. The next moment there was a terrible explosion, destroying the fronts of the neighbouring houses, breaking windows and doors, and tearing up the street to a depth of 4 ft.

On April 3, 1866, a serious explosion occurred in Aspinwall, on Panama's Atlantic coast, in which the steamer *European*, which carried a consignment of nitroglycerin for further dispatch across the Isthmus of Panama, was completely destroyed with a loss of 47 lives and great material damage. Shortly afterwards, in April, 1866, a new explosion occurred in a consignment of nitroglycerin which had been shipped on the same route and had reached San Francisco; 15 lives were lost. Yet another nitroglycerin explosion occurred in Sydney, in Australia, at the same time. Even one of Nobel's earliest factories in Krümmel, outside Hamburg, was destroyed by an explosion in the beginning of May, 1866, while he was in America trying to convince people about the harmlessness of his blasting oil and to acquire patent rights on the product.

In America Senator Chandler, of Michigan, introduced a Bill to "regulate the transportation of nitroglycerin, or glonoin oil," providing that any death caused directly or indirectly by the transportation of this oil on any vessel or vehicle should constitute murder in the first degree and be punished with death by hanging.

These terrible accidents almost threatened to nullify the first great discovery in the explosive field.

They must have caused Alfred Nobel serious disquiet. This was the hard wind from Ardeer which I mentioned in the beginning of my lecture which now was blowing against Alfred Nobel. His brother Robert gave him the following advice: "My good Alfred," he wrote, "give up inventing as soon as possible. It only brings disappointment. You have such wide knowledge and such exceptional qualities that you should turn your attention to more serious matters." The authorities of the City of Stockholm declared after the Heleneborg explosion that if Alfred Nobel wanted to go on with the manufacture he could do it on a barge in the Lake of Mälaren, and do it by himself. And this was what Alfred Nobel did.

The "blasting oil" had become indispensable in railway construction and in the mining industry. They had to have it in spite of the risk.

Dynamite

In the meantime Alfred Nobel experimented intensively in order to make nitroglycerin less dangerous. His efforts finally led to the discovery of dynamite, blasting oil adsorbed by kieselguhr. The diatomaceous earth, a readily available raw material, took up three times its weight of nitroglycerin. The nitroglycerin was thereby stabilized but still explosive on detonation. The dynamite could be safely handled, packed in cartridge form, transported, and stored without risk. As a powder it could be filled in bore-holes from which the liquid blast oil would have flown out. In 1867 this second great discovery was patented in Sweden, and in combination with the earlier detonator provided the first rational technique for the use of explosives. In 1868 Immanuel and Alfred Nobel were jointly awarded the Letterstedt Prize of the Swedish Academy of Science, an honour which Alfred set great store by all his life.

From now on the situation was changed. What for 18 years had been only a chemical curiosity, and recently threatened to become a real danger to humanity, was now transformed by the technically trained Nobel family into one of the most revolutionary factors of the age, making possible mining enterprises previously unheard of, along with railway, tunnel, and canal constructions —for example, the tunnels through the Alps.

Alfred Nobel had now to spend his time in continuous travelling from country to country, for the establishment and supervision of factories and for the acquirement and protection of patent rights. He found use for his cosmopolitan education and solid knowledge of the chief European languages, and, last but not least, for his detailed knowledge of the manufacturing processes. He had talent enough to build a world-wide organization with the capacity to produce the necessary amounts of explosives. During the years 1867 to 1874 the world production of dynamite rose from 11 to 3,120 tons a year.

In spite of these activities a new discovery followed in 1875. It was blasting gelatin, also called rubber dynamite, in which 7% of low nitrated cellulose or collodion had been dissolved in 93% of nitroglycerin, forming a viscous semi-solid mass. The mixture was not so bulky as dynamite, had a greater blasting power, and was totally consumed on ignition.

Ballistite

The next patent was on smokeless gunpowder, the "ballistite," or the Nobel gunpowder, in which nitroglycerin was mixed with an equal part of guncotton (nitrocellulose). It exploded less violently than blasting gelatin, and thereby developed a propellent ballistic force when used in firearms without splitting the barrel. This invention of a propellent explosive, made in 1887, later came to be of the greatest importance in the manufacture of ammunition for firearms and ordnance pieces.

The Cordite Lawsuit

In England Nobel had met with no success in his attempts to get a licence for manufacture. Sir Frederick Abel, an adviser of the House of Commons on matters of explosives, exerted considerable influence in keeping Nobel's nitroglycerin away from England. In 1869 a Nitroglycerin Act was introduced forbidding the import,

storage, and transport of that substance in the country. Only in 1871 was Nobel licensed to erect a nitroglycerin factory in Scotland.

Nobel came into serious conflict with the two inventors of cordite, the physicist James Dewar and Sir Frederick Abel. On the request of a Government Commission Nobel had informed Dewar and Abel, who were members of the Commission, about all the details concerning the patented procedure of manufacturing ballistite. Without regard to this, Dewar and Abel added petroleum jelly to Nobel's nitroglycerin and nitrocellulose mixture, dissolved it in acetone, so that the mass could be drawn out in threads, and patented the product under the name of cordite. Nobel felt compelled to take legal action against them. On the ground that the plaintiff, Nobel, had spoken about the "well-known soluble nitrocellulose" in his claims and the defendants had used the insoluble variety of nitrocellulose, Nobel lost the case. The lawsuit cost him £30,000, and reduced almost to nil the value of the ballistite patent.

One of the judges of the Court of Appeal, Lord Justice Kay, expressed his doubts regarding the justice of the decision. He honoured Nobel by citing the old saying that the dwarf who stands on the shoulders of a giant obviously should see further than the giant himself. "I have in this case," he said, "my sympathies with the original inventor. Mr. Nobel made a great invention, a principally new and extraordinary thing—and then two clever chemists in reading his description discover that they can use the same starting material with only a small difference in one of the components for getting a similar product with exactly the same properties. In fact, through our decision Mr. Nobel has been deprived of an extremely valuable patent." In order to ameliorate the injustice Nobel's Explosive Co., which made the cordite for the British Government, paid Nobel a royalty on its manufacture of cordite amounting to half the amount it paid for the ballistite.

A benevolent act of that kind would, if it had been shown to Nobel in the U.S.A., have made the Nobel Prizes twice as large as they are now, or still larger. In spite of the enormous use of dynamite in the New World, Alfred Nobel benefited very little from it. His fight with the country's unscrupulous financial racketeers, on which he lost much time, was very disappointing to him. The story of this hopeless fight is vividly told by Herta Pauli in her book, *Alfred Nobel, Dynamite King, Architect of Peace*, published in 1942, and by Robert Shaplen (*The New Yorker*, March 15 and 22, 1958). According to Pauli, Nobel lost all interest in his American business.

How close the ties were between Alfred Nobel and the British enterprises in the explosive field was demonstrated in 1918, when the British explosives industry was unified in a single organization, called Explosives Trades Ltd. The organization soon found that the name Nobel signified quality in the industrial world, and therefore changed its name to Nobel Industries Ltd.

Alfred Nobel's Personality

In the Biography of Nobel, edited by the Nobel Foundation in 1926 under the direction of Henrik Schück, it is said of Nobel that he once was jokingly characterized as Europe's richest tramp. Undoubtedly these words contained a certain amount of truth. During the hectic years after his invention of the detonator he travelled from country to country. Mostly he lived in the vicinity of Hamburg, and later in Paris. Sweden, however, still remained his home country, and here he chose his collaborators, among whom the foremost was the engineer Alarik Liedbeck.

Liedbeck was sent to organize the first nitroglycerin plant at Ardeer, where he was succeeded by C. O. Lundholm. Both of them co-operated well with the local industrial and business people, to the benefit of the new enterprise. Lundholm became a naturalized British citizen.

Alfred Nobel never married. All his life he suffered from poor health. The bills for doctors and medicine for Alfred played a large part in the economy of the family during the earlier days. When things changed for the better heavy business obligations occupied all his time. It is said that King Charles XII of Sweden remained a bachelor because of the difficulty of carrying a queen with him on his endless war expeditions in Russia, Poland, and Turkey. The same applies to a certain extent to Nobel. There was also the difficulty of finding an intellectually equal partner; he could not even find a secretary who mastered languages enough to satisfy his demands. "Personally," he said, "I find the conversation of the Parisiennes the dullest there is, while that of educated and not too emancipated Russian women is enchanting. Unfortunately they have an aversion to soap; but one must not ask too much."

Without a family of his own he felt homeless. To his brother Ludwig's wife he once wrote: "What a contrast there is between us. You, surrounded by love, caressing and caressed, anchored in contentment. I, a vagabond, without compass and rudder, like a useless wreck, broken by fate. Without any light memories from the past, without the false but beautiful mirages of the future, created by illusion, without family, which is our only life after death, without friends for the natural cultivation of the heart, without enemies for the cultivation of the gall."

When Ludwig asked for biographical information about their father and Alfred himself, the latter answered: "Why do you want to torment me with biographical essays? No one reads essays except about actors and murderers, preferably the latter, whether they have carried out their impressive deeds at home or in the field of battle." To this he added: "Important things and contractual duties nowadays lie waiting on my desk for weeks, even months, owing to lack of time. In such circumstances it is quite impossible for me to write biographies if they are not as short as a police description; but these are, I think, the most eloquent. For example: Alfred Nobel, a poor semi-alive creature, which should have been suffocated by the doctor as soon as he with a yell made his entry into life. His greatest merits: to keep his nails clean and never be a burden to anybody. Greatest fault: to lack a family, good temper, and good stomach. His greatest and only demand: not to be buried alive. Greatest sin: not to worship Mammon. Important events in his life: none."

Nobel and the Peace Movement

During the first twenty years following his discovery of the detonator and of dynamite Alfred Nobel's activities were exclusively limited to the manufacture of nitroglycerin and dynamite, including the rubber dynamite for application in the fields of mining and

in road, canal, and tunnel constructions. The most remarkable improvements in people's living conditions had thereby been achieved. Nothing could be more misleading than to label Alfred Nobel as a "merchant of death," as has been done. His fortune was collected during these first twenty years. It was not until the middle 'eighties that his gunpowder manufacture was any part of his business.

Being highly intellectual and strongly influenced by the humanistic tendencies of contemporary literature, with a keen eye for the weaknesses of the political systems of his time, Alfred Nobel could not avoid getting involved in the discussion about war and peace. His discoveries had opened unlimited possibilities for destructive wars, and the great Powers cultivated a hostile attitude towards each other. He said, "If in thirty years we shall not have succeeded in reorganizing the world, it will inevitably relapse into barbarism." As it actually did.

Nobel himself thought that the only chance of peace lay in the opposing powers hesitating before the risks involved. When Bertha von Suttner, who in 1889 published *Lay Down Arms*, asked for money for the Peace Congress in Berne in 1892, she received a sum, but Nobel did not believe that the congress could be of any particular value. "I believe," he said, "that my factories will put an end to war sooner than your congresses. When the day dawns, when two army corps can destroy each other in one second, all civilized nations will surely recoil from war in horror and disband their armies." At least, he said, the governments would postpone hostile actions for a year or two, hoping that the air would clear in the meantime, some politicians might possibly die, and common people would have time to think it over before starting the bloody business. If this should fail, an international court and a collective defence system should be applied against an aggressor. "Wars will become impossible when all states bind themselves absolutely to take action against the first aggressor." Nobel expressed his great esteem for Bertha von Suttner's writings against war and armaments, but he still retained his belief that in some situations a collective attack on an aggressor might become necessary.

Even if Nobel did not trust very much in the efficiency of peace congresses he finally decided to design the Peace Prize in his will "for the person who shall have done the most effective work for promoting friendly relations between the peoples, for the abolition or reduction of standing armies and for the formation and popularization of peace congresses." Being a practical man, he fully understood that the best way of putting dynamite under the warmongers was to create friendly relations among the inhabitants of neighbouring countries, a principle successfully applied for the first time in the history of Europe nine years after his death, when the union between the Scandinavian brother-countries Sweden and Norway was dissolved. It was an intelligent step Nobel took when he put the awarding of of the Peace Prize in the hands of the Norwegians, the "rebels" that urgently demanded to have the union with Sweden broken.

The Will

When Nobel, in the 'nineties, felt that it was time to write his will and dispose of a fortune amounting to 33 million Swedish crowns, he decided that the money should be used for the benefit of society. The witnesses to the will later said that they have heard him say on the occasion of signing: "At heart I am a social-democrat, in moderation. I especially believe large inherited fortunes to be a misfortune which only serves to stupefy humanity. A person who owns a large fortune should, therefore, only allow a small part of it to fall to his relatives." He considered it wrong to leave even direct heirs more than they need for education, or to let them have a larger sum than they have earned themselves. To act differently, he thought, would mean encouraging indolence and preventing a healthy development of the individual's capacity to create an independent position for himself.

The content of his will is very well known. He stated that:

"With the residue of my convertible estate I hereby direct my Executors to proceed as follows: They shall convert my said residue of property into money, which they shall then invest in safe securities; the capital thus secured shall constitute a fund, the interest accruing from which shall be annually awarded in prizes to those persons who shall have contributed most materially to benefit mankind during the year immediately preceding. The said interest shall be divided into five equal amounts, to be apportioned as follows: One share to the person who shall have made the most important discovery or invention in the domain of Physics; one share to the person who shall have made the most important Chemical discovery or improvement; one share to the person who shall have made the most important discovery in the domain of Physiology or Medicine; one share to the person who shall have produced in the field of Literature the most distinguished work of an idealistic tendency; and, finally, one share to the person who shall have most or best promoted the Fraternity of Nations and the Abolishment or Diminution of Standing Armies and the Formation and Increase of Peace Congresses."

Nobel made up his will and signed it on November 27, 1895. It is known that his distaste for lawyers was so great that even on this exceptional occasion he refused to ask for legal advisers, consequently many formalities were overlooked.

But it was not only against the law people he could be sarcastic. He had all his life to pay attention to his health, and came thereby in contact with medical men and medical problems. He was well aware of the weaknesses of the medical sciences. When in his older days he consulted, as he put it, two "fakultets-åsnor," one of them told him that he was suffering from rheumatic gout and the other spoke about gouty rheumatism. Both prescribed for him to take his own blasting oil, nitroglycerin, to find relief from his cardiac pain.

As to his will, the question came up of where Nobel had his domicile. Since his ninth year he had not been registered anywhere. It is not surprising that the French tax-collecting department, "le Fisc," showed a special interest in his fortune. Fortunately, he became registered in Sweden in 1894, when he bought the Bofors arms firm. But for this formality, his fortune would certainly have stayed in France to be liquidated during the economic chaos in Central Europe which followed in the period after his death.

Nor were the governing bodies who should award the Prizes asked beforehand if they were able or willing to accept the offer. It thus happened that the Swedish Academy of Science, which now awards the Prizes for Physics and Chemistry, felt unable to select

representatives even for preliminary discussions with the executors of Alfred Nobel's will until it was evident that the will would become legally recognized. Leading conservative politicians in Sweden declared the will as an infringement of the legal rights of Nobel's heirs.

Meanwhile some of Nobel's heirs in Sweden had brought an action against the executors, claiming that the will should be declared invalid. The executors of the will appointed by Nobel, Mr. Ragnar Sohlman and Civ.eng. Rudolf Lilljequist, would have met an almost insurmountable resistance from the authorities and the heirs had not the nephew of Alfred Nobel, Ludwig's son Emanuel Nobel, in February, 1898, declared that he, although the death of Alfred Nobel had heavily shaken the financial ground of the naphtha enterprises in Russia, was willing to do his best to see that his uncle's will should be respected. The action of Emanuel Nobel on this occasion deserves to be remembered. Such a disregard of what was considered the rights of the heirs as Alfred Nobel had shown was in fact unheard of. Because of the extraordinarily good relations which had always prevailed within the family, Emanuel felt convinced that deeper motives had induced his uncle's decision. He therefore, when the highest representative of the State claimed that Alfred Nobel had been "influenced by peace fanatics and particularly by women" and advised him to act in favour of the heirs' rights, responded: "Your Majesty! It is not my intention to take any action through which members of my family in the future could be blamed by the most highly deserving scientists of the time for having deprived them of something which duly ought to be theirs."

Emanuel Nobel called the executors "solicitors of the soul." He participated in the preliminary discussions between them and the representatives of the Swedish Academy and the Karolinska Institutet. A proposal was made on June 5, 1898, according to which the heirs should be allotted one and a half years' income to the estate, provided they recognized the will and waived any further claims upon the estate. To this they agreed, and thereby the estate was saved for the Nobel Foundation, whose Articles were approved by His Majesty the King in June, 1900. The following year, 1901, the first Nobel Prizes were awarded.

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The Department of Scientific and Industrial Research will take over part of the former Royal Ordnance Factory at Thorp Arch, near Boston Spa, Yorkshire, for the use of the new National Lending Library for Science and Technology. Present plans are that the library will begin work at Thorp Arch in 1961, becoming fully operational during the following year. The new library—the nucleus of which already exists in the D.S.I.R. Lending Library Unit now at Chester Terrace, Regent's Park, London—will cover all subjects in science and technology, except for some fields of medicine. One important activity will be the expansion of work on the translation of Russian scientific literature, now organized by the Lending Library Unit in collaboration with the National Science Foundation in the United States.

ACUTE PANCREATITIS

ANALYSIS OF 100 PATIENTS

BY

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For a good many years the General Infirmary at Leeds has accepted most of the emergency surgical patients from this city (population 508,000) and the immediately surrounding countryside. The number of acute surgical admissions, excluding head injuries, has been fairly constant over the past six years at 2,300 to 2,600 per annum. During this period 100 patients with acute pancreatitis have been admitted. A further 41 patients have been seen whose serum amylase was raised but in whom the diagnosis of acute pancreatitis was either doubtful or erroneous. It is with this series of 141 patients that the present communication deals.

Aetiology

There are two schools of thought about this unsolved question. The first school is the older, and its two chief exponents have been Opie (1903) and Rich (see Rich and Duff, 1936). At necropsy on a patient who had died of acute pancreatitis Opie found a stone in the ampulla of Vater, blocking the common orifice of biliary and pancreatic ducts and converting them into a continuous channel. He postulated that an increase in biliary pressure would force bile up the pancreatic duct, where it would activate trypsinogen and cause pancreatic necrosis. The second part of this theory he proved by causing acute pancreatitis in dogs by injecting their own bile into their pancreatic ducts. The first postulate, that pressure in the biliary duct must exceed that in the pancreatic duct, has been more difficult to establish. In fact, the most reliable work on biliary and pancreatic duct pressures (Parry, Hallenbeck, and Grindlay, 1955) shows that biliary secretory pressure in dogs almost never exceeds pancreatic secretory pressure. These results may not be applicable in man, however, since the anatomy of the ducts is so different in dogs, the main pancreatic duct opening a centimetre or more below the common bile duct.

It was soon realized that it is unusual to find a stone impacted at the ampulla of Vater in patients with pancreatitis. In the present series 26 patients died. Of these, 22 were examined *post mortem*, and in five a stone was found impacted at the ampulla of Vater. In addition, in one patient operated on during an attack of acute pancreatitis a stone was found at the ampulla and removed. In the remaining cases it has been postulated that the common biliary-pancreatic pathway is established by spasm of the sphincter of Oddi. This is the theoretical background to sphincterotomy in the treatment of chronic relapsing pancreatitis.

In 1936 Rich and Duff published their researches on the pathology of pancreatitis and described a form of pancreatic duct mucosal hyperplasia which they believed could cause obstruction. They postulated that over-secretion by the pancreas against a blocked duct could cause pancreatitis. On the other hand, pancreatography in patients with pancreatitis shows that obstruction to the duct anywhere except at the sphincter of Oddi is exceedingly uncommon (Doubilet, Poppel, and Mulholland, 1957; Pollock, 1958).

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The second school of thought regarding pancreatitis considers that the primary lesion is in the nature of a pancreatic infarct, and that the escape of pancreatic juice is secondary to this. Perhaps the most interesting work along these lines is that of Thal and Brackney (1954), who liken the lesion to a Shwartzman phenomenon and have produced it in rabbits and goats by intraductal, followed 24 hours later by intravenous, injection of meningococcal or *Escherichia coli* endotoxin. The clinical significance of these results is not clear, and one must conclude that ductal obstruction with or without biliary regurgitation plays the major part in causing most cases of human pancreatitis.

Clinically, certain facts about aetiology emerge from a consideration of the present series.

Age and Sex

Of the 100 patients 71 were female and 29 male. There is an extraordinarily wide age variation. The youngest patient was a boy of 6 years:

Case 1.—A boy aged 6 was admitted to hospital as a case of acute appendicitis. Four days before admission he had had abdominal pain and vomiting, which was repeated on the day of admission. The pain did not radiate to the back. There was no history of mumps or any exposure to a case of mumps. No child in the ward subsequently developed that condition. At laparotomy on the day of admission widespread fat necrosis and a grossly oedematous enlarged pancreas were found. The abdomen was closed and the child made a good recovery. The serum amylase was 6,400 units (Somogyi) on the day after operation, and was still raised to 1,800 units four days later. A mumps complement-fixation test was not done. The child was well four years later.

A similar case in a girl of 3 years was reported by Pender (1957). The oldest patient in the present series was aged 83, and the numbers by decades were: first, 1; second, 2; third, 8; fourth, 4; fifth, 11; sixth, 19: seventh, 33; eighth, 19; and ninth, 3.

Association with Gall-bladder Disease

This was less common amongst the men: the gall-bladder was normal in 14, abnormal in 13, and in two there is no information. Of the women, 48 had abnormal and 16 had normal gall-bladders, and in 7 its state was not known. In brief, half the men and three-quarters of the women had abnormal gall-bladders. In most cases the abnormality was the presence of cholecystitis with stones; in some, however, no stones were present (see Fig. 1), but only an acute cholecystitis. In such a case the gall-bladder may fail to concentrate cholecystographic dye during the attack of pancreatitis, only to appear completely normal later.

FIG. 1.—Gall-bladder removed *post mortem* from a woman who died of acute haemorrhagic pancreatitis. Note the patchy ulceration of acute non-calculous cholecystitis.

This strong association between disease of the gall-bladder and of the pancreas is difficult to explain on any present theory of the aetiology of pancreatitis, especially as only six patients were shown to have stones impacted at the lower end of the common bile duct. It is possible that the functional removal of the gall-bladder by cholecystitis or cholecystectomy may allow a higher pressure to develop in the common bile duct, and that this pressure, exceeding that in the pancreatic duct, may drive bile up the pancreatic duct to initiate an attack of acute pancreatitis. Menguy, Hallenbeck, Bollman, and Grindlay (1955) have shown in dogs that pressure in the common bile duct rises considerably after cholecystectomy and in one dog it exceeded the pressure in the pancreatic duct.

Other Factors

Alcohol.—In not one single patient in the present series was there any association with alcoholic excess, in contrast to the experience in several American clinics—for example, Puestow and Gillesby (1954).

Food.—No constant time relation was noted between the ingestion of food and the onset of an attack of acute pancreatitis. In a number of patients pre-existing intolerance to certain foods, notably fats, was found.

Operations.—Apart from two patients whose pancreatitis was induced by transduodenal sphincterotomy and pancreatography (this series is to be published elsewhere), there was only one example in the present series of post-operative pancreatitis, such as that of Kirby, Senior, Howard, and Rhoads (1955). We have not found acute pancreatitis as an immediate complication of partial gastrectomy.

Case 2.—A woman of 57 had a right lower parathyroid adenoma excised for classical hyperparathyroidism. She became shocked and anuric the following day, and died nine days later with a serum calcium of 6.2 mg. per 100 ml. At necropsy acute haemorrhagic pancreatitis was found.

Rare Causes

Rare causes of acute pancreatitis include traumatic rupture of the pancreas and pancreatic carcinoma. There was one case of the former and two of the latter association in this series.

Case 3.—A man of 27 was accidentally struck across the upper abdomen by a heavy steel file. This was almost immediately followed by abdominal pain and vomiting. Twelve hours after the injury he was admitted with a diagnosis of a ruptured viscus. At laparotomy much fat necrosis was found, together with a haemorrhagic ascites, and an area of bruising and intense fat necrosis at the upper border of the middle of the pancreas. A drain was led down to this region, and post-operatively he developed jaundice and a pancreatic fistula which discharged for eight weeks and then cleared up. The serum amylase on the day after operation was 3,000 units per 100 ml. (Somogyi). Three years later he is in good health and has had no recurrence of abdominal pain.

Case 4.—Fifteen months after a cholecysto-jejunostomy for obstructive jaundice, a man of 39 developed steatorrhoea, vomiting, and upper abdominal pain. His serum amylase was 1,800 units per 100 ml. He died of gastrointestinal haemorrhage, and necropsy showed a carcinoma of the head of the pancreas, considerable dilatation of the obstructed pancreatic duct, an abscess in the tail of the pancreas, and a large pseudopancreatic cyst.

Case 5.—A woman of 61 had had four attacks of severe upper abdominal pain and vomiting in the five months

preceding her admission. She had a fixed mass in the epigastrium and her serum amylase was 1,160 units per 100 ml. At laparotomy gross enlargement of the head of the pancreas was found. There was a little fat necrosis, and the mass was obstructing the second part of the duodenum. A posterior gastro-jejunostomy was done. She soon became jaundiced, and a cholecysto-jejunostomy was performed. She went rapidly downhill, dying five months after the first operation. Necropsy was not performed and there is no pathological proof of carcinoma in this case, but the clinical course and operation findings are highly suggestive.

Pathology

The differentiation into oedematous and haemorrhagic pancreatitis is arbitrary, and often it is possible, in a pancreas which on the surface shows only oedema, to demonstrate haemorrhage within the substance.

In a few of the patients in this series transduodenal pancreatography has been performed, and has shown that during an attack of acute pancreatitis there is an escape of injected fluid from the ducts, with diffuse opacification of the gland substance. After recovery from an acute attack no entirely characteristic changes have been found, although the pancreatic ducts are usually wider than normal. This method has been abandoned because of its limited value and considerable danger.

In general, especially in the more severe forms of the disease, the onset is explosive and can be likened to a rupture of the pancreas. Activated trypsin, lipase, and amylase are liberated in large quantities into the blood stream, the peritoneal cavity, and the retroperitoneal tissues. Whether the circulation of these enzymes in the blood stream, where their presence can be fairly easily detected by chemical tests, is responsible for any of the general changes of acute pancreatitis is debatable. The evidence points to the conclusion that most of the general effects can be attributed to loss of circulating fluid into the peritoneum and retroperitoneal tissues (Pollock, 1956). There is, however, an isolated case report (Vogel, 1951) of cerebral demyelinization and focal necrosis in organs, particularly the myocardium, in a patient who died of acute haemorrhagic pancreatitis. These lesions probably resulted from the action of circulating trypsin. It is not unlikely (Pollock and Bertrand, 1956) that the electrocardiographic changes which are sometimes found in acute pancreatitis are due to the same cause. The presence of active pancreatic enzymes in the peritoneum and retroperitoneal tissues causes striking effects, notably tissue necrosis and haemorrhage and fat necrosis. Occlusion of the foramen of Winslow may allow the development of a pseudo-pancreatic cyst.

Twenty-five patients with acute pancreatitis were operated on within the first week. In ten of them either a bile-stained ascites or bile staining of the peripancreatic oedema was noted. In the remainder, either the colour of the fluid was not noted or it was said to be haemorrhagic. This observation lends some support to Opie's theory of bile reflux as a cause of the disease.

Occasionally there appears to be an upward extension of pancreatic enzymes, and three patients at necropsy were found to have lesions above the diaphragm which were probably the result of pancreatic enzyme activity. In one there was considerable fat necrosis in the anterior mediastinum, in the second fat necrosis in the posterior mediastinum, and in the third a blood-stained pericardial effusion.

In other cases downward movement of the digestive juices results in necrosis, haemorrhage, and fat necrosis in the right iliac fossa. There were three patients who presented with fixed masses in the right iliac fossa due to the sealing off of such an area.

Case 6.—A woman of 67 was admitted to hospital with a diagnosis of acute appendicitis and a history of severe abdominal pain and vomiting for 24 hours. She was found to be ill, and the right iliac fossa region was tender and rigid. At laparotomy there was a retroperitoneal liquid haematoma in the right iliac fossa, a slightly blood-stained ascites, and a hard enlarged pancreas with some peri-pancreatic fat necrosis. Her recovery was slow but ultimately satisfactory. Three years later she was found to be diabetic. Six years after the operation, she enjoys good health, has a little flatulence, and has to avoid certain foods. Her diabetes is kept under control with insulin.

Case 7.—A man of 70 was admitted to hospital with a diagnosis of strangulated right interstitial inguinal hernia. For nine days he had had some colicky abdominal pain and pain in the back. He had vomited frequently. A large tender mass, which felt fairly superficial, was found above the right inguinal ligament in its lateral half. When the patient was anaesthetized a second fixed mass 3 in. (7.5 cm.) in diameter was felt in the epigastrium. This was thought to be pancreatic. It gradually disappeared over the next four weeks. On incising the mass in the right iliac fossa about 200 ml. of sterile inoffensive clear fluid containing white flecks was liberated, leaving a cavity with shaggy bile-stained walls, in which were spots of fat necrosis. The cavity continued to drain for nearly three months. When seen a year later the patient was in excellent health and had no symptoms of any kind.

Case 8.—A woman of 53 was admitted to hospital with a diagnosis of acute pancreatitis. On the day before admission she had been seized with a violent epigastric pain which lasted nearly two hours and then departed for 16 hours. It then returned, radiated through to the back, and was accompanied by vomiting and mild diarrhoea. She was found to be reasonably well generally, with tenderness and rigidity in the upper abdomen. Her serum amylase was 1,900 units per 100 ml. (Somogyi), blood urea nitrogen 47.2 mg. per 100 ml., and serum bilirubin 1.6 mg. per 100 ml. She made a slow but satisfactory recovery. A week after admission a tender hard fixed mass was felt in the right iliac fossa. This gradually resolved. Five months later her gall-bladder (which contained stones) was removed, and the region of the right iliac fossa was examined. There was still a small partly liquid haematoma present in the retroperitoneal tissues. The pancreas was firm. A year after the operation she was well but had to avoid fatty foods.

So far as the pancreas itself is concerned, the extent of necrosis varies considerably. If it is minimal, in the so-called oedematous type of pancreatitis, resolution may be complete within a short time. More extensive necrosis may heal by fibrosis, and may involve enough islets to lead to diabetes, or may cause obstruction to the common bile duct or the pancreatic duct. Finally, the whole or part of the pancreas may become liquefied, leading to one variety of true pancreatic cyst or abscess.

Symptoms and Signs

Classically, an attack of acute pancreatitis is heralded by the sudden onset of severe constant abdominal pain radiating through to the back and accompanied by frequent vomiting. The vomitus contains bile but rarely frank small-intestinal contents. It is seldom foul-smelling. Only 10 of the 100 patients had no history of vomiting. The nature of the pain was, however, rather more variable. Four patients were comatose on admission and died soon after, and one was anuric

on admission and died soon after; all the remaining 95 patients had abdominal pain. This could be classed as one of three types: sudden onset of pain radiating to the back, 61 patients; sudden onset of pain not radiating to the back, 18 patients; gradual onset of pain with or without radiation, 16 patients.

The exact situation of the abdominal pain also was variable. It might be epigastric, right or left hypochondrial, or lower abdominal. It was usually sharp and severe, though occasionally colicky. It usually responded fairly quickly to bed rest and analgesics unless a pseudo-pancreatic cyst formed, when the pain might be unrelenting and severe.

Physical signs were extremely variable. Most of the patients were well nourished, but obesity was not usually a feature.

The classical picture of acute pancreatitis—the pallor, sweating, cyanosis, low blood pressure, oliguria, and abdominal tenderness and rigidity—was present in about half the patients. Sometimes the general signs of shock due to fluid loss dominated the picture and suggested a diagnosis of myocardial infarction. In four patients the general signs were unassociated with local signs, the patients being comatose and dying within a short time.

The most common erroneous provisional diagnosis was a perforated peptic ulcer, which was made in 29 patients: 16 of these patients were operated on. In the remaining patients both general and local signs were milder and the differential diagnosis lay between cholecystitis, appendicitis, and pancreatitis.

Staining of the flanks was found in only one patient, and this and peri-umbilical staining are regarded as rare and unreliable signs of acute pancreatitis.

Diagnosis

With increasing use of the simple starch-digestion test for amylase in the serum, the accuracy of diagnosis has considerably improved. Of the 100 undoubted cases of pancreatitis, 9 were incorrectly diagnosed until necropsy, 35 were incorrectly diagnosed until laparotomy, and 56 were correctly diagnosed by the clinical picture and estimation of the serum amylase.

The incorrect diagnoses made in patients who came to necropsy were: coma of uncertain origin in four, anuria due to parathyroidectomy in one, myocardial infarction in two, peritonitis of unknown cause in one, and acute cholecystitis in one.

When the correct diagnosis was established by operation a provisional diagnosis of perforated peptic ulcer had usually been made (16 patients). Less common errors were acute cholecystitis (nine patients), acute appendicitis (one patient), and strangulated interstitial hernia (one patient).

Electrocardiographic Changes

It is by no means uncommon to find an abnormal electrocardiogram showing decreased voltage of T waves, sometimes inversion of T, and occasionally depression of ST during the course of acute pancreatitis. Thirty-two patients in the present series have had electrocardiograms taken during their attack. In 19 of these the record was abnormal, in two of them so abnormal as to support a provisional diagnosis of myocardial infarction. One of these patients died.

Case 9.—A woman of 59 was admitted as an emergency case. On the day of admission she had had a sudden attack of severe upper abdominal pain which radiated into the left side of the chest and down the left arm. The left hand became cold and blue. She had vomited many times. A similar attack had occurred 10 months previously. She was found to be shocked and cyanosed, and had some upper abdominal tenderness and rigidity. A diagnosis of myocardial infarction was supported by the electrocardiogram, which showed inversion of T in lead I and slight depression of ST (see Fig. 2). The changes were thought to

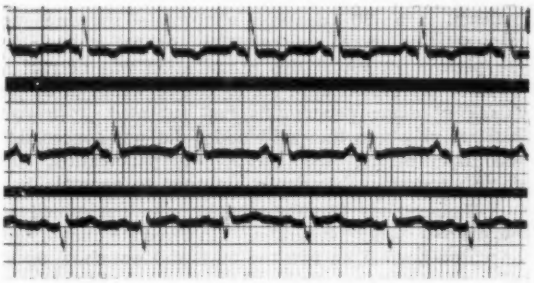

FIG. 2.—Case 9. Electrocardiogram, leads I, II, and III. The inversion of T wave in lead I and the slight ST depression were thought to be in keeping with an antero-septal myocardial infarct. At necropsy the heart was normal and the pancreas was destroyed by acute haemorrhagic pancreatitis.

be in keeping with a recent antero-septal infarct. The patient was treated with heparin and phenindione ("dindevan"), and died a week after admission. At necropsy acute haemorrhagic pancreatic necrosis was found, with extensive fat necrosis in the peritoneal cavity. The gall-bladder contained four small faceted stones. The heart showed no infarction, and the aorta and coronary arteries were practically free from atheroma.

The electrocardiographic changes disappear with recovery of the patient and may return in identical form in subsequent attacks (see Fig. 3).

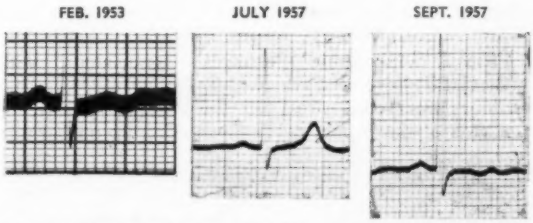

FIG. 3.—Electrocardiogram, lead V4. In February, 1953, this woman of 48 had an attack of acute pancreatitis which produced a biphasic T wave. In July, 1957, she was symptom-free and the T wave had returned to normal. In September, 1957, she had another attack of pancreatitis, which again caused a T-wave change.

The origin of these abnormalities is obscure. They are not specific, as similar changes may be found in the presence of upper abdominal peritonitis from other causes (see Case 12) and may be induced by manipulation of the gall-bladder and bile ducts (Gubner, 1944). Evidence has been presented (Pollock and Bertrand, 1956) that similar changes may be produced by intravenous injection of trypsin or pancreatic juice in dogs. The changes are not due to oligaemia or to hypokalaemia.

Radiological Diagnosis

Sixty-five patients were examined radiographically at some time during the course of their illness.

1. Plain films of the abdomen were taken in the erect and supine positions in 38 patients: in 29 the films were normal; in three the presence of gas and fluid levels in small and large bowels denoted paralytic ileus; in three

there was elevation and poor movement of the right leaf of the diaphragm and in one of the left leaf; in two opaque gall-stones were seen. All films have been reviewed to discover the incidence of the "colon cut-off sign" (Stuart, 1956). In every case in which the films were of adequate quality the sign was negative and it was possible to see gas or faeces in the transverse colon.

2. Oral cholecystography was carried out in 38 patients. In 30 it was abnormal, showing no concentration, poor concentration, or gall-stones. In the patients in whom this examination was normal it was not performed until six to twelve weeks after the attack of acute pancreatitis had subsided. In two patients in whom the gall-bladder did not concentrate the dye during the attack of pancreatitis, the cholecystogram subsequently returned to normal.

3. Intravenous cholangiography was performed in six patients, using "biligrafin." In three the duct system appeared normal, in two the ducts did not show up at all, and in one the common bile duct was dilated.

4. Barium-meal radiography was performed in 26 patients. In 13 it was normal (three of these patients were examined within a week of the onset of pancreatitis). In eight the stomach was grossly displaced forward by a retrogastric mass, which in six patients was a pseudo-pancreatic cyst (see Fig. 4), in the remaining two there was merely a swollen pancreas. In five an abnormality of the mucosal pattern in the stomach or duodenum was found (see Fig. 5). This abnormality was shown in two of the five patients to be due to oedema of the mucosa of the stomach where it was in contact with the inflamed pancreas. The close resemblance to an infiltrating carcinoma of the stomach is obvious and caused great diagnostic difficulty at the time. In one patient an upper jejunal obstruction was found, shown subsequently to be due to multiple adhesions to plaques of fat necrosis.

The radiographic changes associated with pancreatitis have been reviewed by Poppel (1954). That author lays some stress on the "papillary sign"—oedema of the papilla of Vater showing up on barium-meal *x*-ray examination as a filling defect in the second part of the duodenum. It is usually associated with oedema of the surrounding duodenal mucosa and with irritability of the duodenum, stomach, and upper jejunum. This change was found in two of our patients, and it may be more common if the examination is carried out early in the course of the disease.

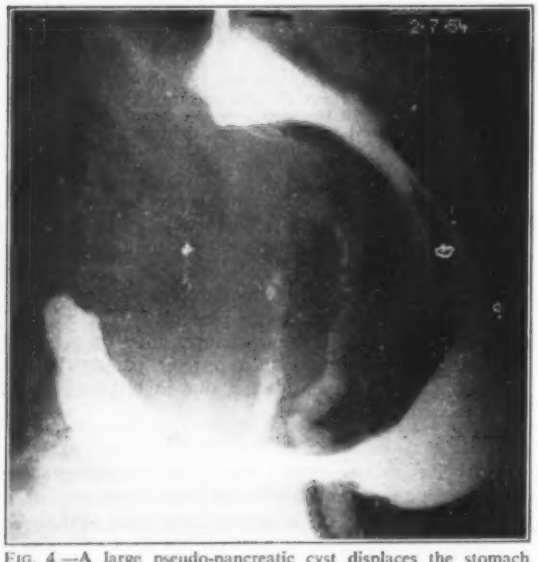

FIG. 4.—A large pseudo-pancreatic cyst displaces the stomach forwards in this barium-meal lateral radiograph. The patient had a fatal cardiac arrest during the performance of cysto-gastrostomy.

FIG. 5.—Gross irregularity of the gastric mucosal pattern due to oedema of the stomach wall where it was adherent to an acutely inflamed pancreas. The appearance is consistent with carcinomatous infiltration, but it became normal after the attack of pancreatitis had settled down.

Biochemical Diagnosis

Somogyi's method of estimation of the time taken to digest a standard starch solution has been used. In our laboratory the upper limit of normal has been 200 units per 100 ml. of serum.

Serum Amylase between 200 and 600 units per 100 ml.—There were 16 patients with pancreatitis whose serum amylase did not exceed 600 units per 100 ml. In 11 of these the diagnosis was confirmed by operation, in one by necropsy, in one by the development of staining of the flanks (Grey Turner's sign). In the remaining three the clinical picture and course were typical of pancreatitis. During the same period 34 patients have been seen whose serum amylase lay between 200 and 600 units per 100 ml. but in whom the diagnosis of acute pancreatitis was either erroneous or not proved. Seven of these patients had acute cholecystitis with gall-stones. Three had previously had a cholecystectomy, and attacks of upper abdominal pain the cause of which remained obscure. In 12 no satisfactory diagnosis was reached. In the remaining patients the following diagnoses were made: carcinoma of the pancreas (2), cirrhosis of the liver, tuberculous peritonitis, acute appendicitis, ruptured ovarian cyst, aortic aneurysm, myocardial infarct, immediately following gastrectomy, duodenal ulcer, perforated duodenal ulcer (2).

Serum Amylase over 600 units per 100 ml.—This was found in 71 patients with pancreatitis (in the remaining 13 no estimations were done, the diagnosis being made at operation or necropsy). There were in addition eight patients in whom serum amylase estimations lay above 600 units per 100 ml. who were shown not to have pancreatitis. These cases are so important from the point of view of differential diagnosis that each is described below:

Case 10: Perforated Gastric Ulcer.—A man of 60 was admitted to hospital with haematemesis and melaena. A week later he complained of severe upper abdominal pain radiating to the back, with vomiting. His serum amylase was 1,300 units per 100 ml. He was treated conservatively and died the next day. At necropsy a perforated high gastric ulcer and anterior and posterior duodenal ulcers were found. There was no evidence of pancreatitis.

Case 11: Intestinal Obstruction.—A man of 36 had a partial gastrectomy for duodenal ulcer. He was well until

three years later, when he gradually developed abdominal pain and vomited once. He was found to be cyanosed and collapsed, with an unrecordable blood pressure, a haemoglobin of 19.6 g. per 100 ml. (135%), and a serum amylase of 1,600 units per 100 ml. He was treated by aspiration and intravenous fluids on a diagnosis of acute pancreatitis until three days later, when he vomited faeculent fluid. At laparotomy a band obstruction of the lower ileum was found with a non-viable upper constriction ring. This was resected, but he developed septic complications and died two months later.

Case 12: Intestinal Strangulation.—A woman of 68 was admitted to hospital with a strangulated right femoral hernia. This was reduced and repaired. Four days later she collapsed and her serum amylase was 2,000 units per 100 ml. An electrocardiogram showed Q waves in leads III and VF, with some ST elevation in these leads and in lead II. She died next day, and necropsy showed that the reduced loop of bowel had become gangrenous and had perforated. The pancreas and heart were normal.

Case 13: Empyema of Gall-bladder.—A woman of 66 was admitted to hospital with an attack of severe upper abdominal pain and vomiting. Her serum amylase was 750 and 1,070 units per 100 ml. on two separate days, and she was treated conservatively on a diagnosis of acute pancreatitis. By the fourteenth day she had not recovered, and at laparotomy an empyema of the gall-bladder was found. The pancreas felt normal and there was no fat necrosis. Following cholecystectomy she made a good recovery.

Case 14: Stone in Common Bile Duct.—A man of 72 complained of recurrent attacks of severe epigastric pain radiating to the back and associated with vomiting. During the most recent attack he became jaundiced. His serum amylase was 710 units per 100 ml. He made a good recovery and operation was not advised. A year later, however, he had another severe attack of pain, vomiting, and jaundice, and at operation stones were found in the gall-bladder and one in the common duct. The pancreas appeared normal.

Case 15: Myocardial Infarction.—A woman of 64 collapsed with tight precordial pain and vomiting. Her serum amylase was 400 and 650 units per 100 ml. on two separate occasions. Her electrocardiogram showed an inverted T wave and elevated ST in leads V1 to V4, and she was treated for antero-septal myocardial infarct. She made a good recovery, but her subsequent history is not known.

Case 16: Ruptured Ovarian Cyst.—A woman of 28 was admitted to hospital as a case of acute appendicitis with a history of sudden onset of lower abdominal pain, without radiation to the back or vomiting. She was tender in the lower abdomen, and a serum amylase estimation was 1,100 units per 100 ml. She was treated conservatively and made a good recovery. Eleven months later she was readmitted with a similar attack; laparotomy was done, and a ruptured chocolate cyst of the left ovary was found. The right ovary was also affected and both ovaries were removed. Two years later she was well.

Case 17: Myocardial Infarction.—A woman of 86 had had a myocardial infarct diagnosed eight years previously. She made a good recovery and led a moderately active life until four days before her admission as an acute case, when she developed a sudden severe precordial and epigastric pain radiating into both sides of the back. She vomited several times. On examination four days later she was moribund, with a blood pressure of 85/60 mm. Hg, and was tender in the epigastrium. An electrocardiogram showed low voltages but no specific abnormality, and the serum amylase was 800 units per 100 ml. She died next day, and at necropsy the pancreas was normal; the left ventricular myocardium was occupied by an enormous recent infarct 8 cm. in diameter.

Complications

Jaundice.—Thirty-two patients developed clinical or latent jaundice. Recently this has been found much more commonly as a result of estimating the serum bilirubin in all patients with pancreatitis. Only five patients have been found in whom this estimation was within normal limits. In general the jaundice tends to subside with the pancreatitis and it is likely that it is an obstructive phenomenon due to the swelling of the head of the pancreas.

Diabetes.—Three patients were known to be diabetic before the onset of their attack of acute pancreatitis. In one the condition deteriorated after the attack, as judged by the amount of insulin required, and in the other two it remained unchanged. Fourteen patients were discovered to have high fasting blood sugars or diabetic glucose-tolerance tests during or after their attacks of pancreatitis. That it should complicate the more severe forms of the disease is understandable, and is attested by the fact that no fewer than 8 of these 14 patients died. Two of the surviving patients require insulin, one does not, and in three the follow-up period is too short to be sure. It does appear, however, that the diabetes is permanent in each case.

Tetany.—The serum calcium was estimated in 36 patients during their attack of pancreatitis. In 30 the figure lay between 8.5 and 11 mg. per 100 ml. (normal). Four of these patients died. In six patients the serum calcium lay between 5.6 and 8.2 mg. per 100 ml. All these patients developed clinical tetany and they all died, despite massive intravenous administration of calcium in the form of calcium gluconate. The explanation for the low serum calcium which is generally accepted is that the fat in the areas of fat necrosis is hydrolysed by lipase to fatty acids and glycerol. The former combine avidly with ionized calcium to form calcium soaps, and the blood-bone calcium balance is upset. The association between tetany and a fatal outcome is so strong, however (see also Edmondson and Berne, 1944), that this explanation cannot be the whole truth.

Electrolyte Disturbance and Uraemia.—For a variety of reasons, including vomiting, paralytic ileus, ascites, and pancreatic fistula, patients with a severe attack of pancreatitis are liable to disturbances of fluid and electrolyte balance and thence to extrarenal uraemia. There were 17 such patients in the present series, of whom 12 died. The chemical findings showed nothing characteristic, and acidosis was as common as alkalosis. On the whole the response to treatment was poor.

Anaemia and Hypoproteinaemia.—In nine patients a "secondary" type of anaemia became manifest during the course of the illness and responded to blood transfusions. Two of these patients also had hypoproteinaemia, and they both died. It is likely that minor degrees of anaemia were overlooked in many patients.

Gastro-intestinal Haemorrhage.—Three patients had a haematemesis or melaena during the course of acute pancreatitis. Two of these died; in one no lesion was discovered in the stomach or duodenum; in the other no necropsy was allowed, but an ante-mortem barium-meal *x*-ray examination had shown a gastric ulcer. In addition a patient with a pseudo-pancreatic cyst was found to have a gastric ulcer.

Masses and Pseudo-cysts.—Twelve patients developed a clinically palpable mass during their illness. In 10 this was epigastric, in one in the right iliac fossa; and one patient (Case 7) had a mass in both situations. In

two the pancreatitis was secondary to carcinoma of the pancreas and no direct attack on the mass was made. In two it resolved spontaneously. The remaining pseudo-cysts were drained, five into the stomach and four to the exterior. One in each group died—the patient with gastro-cystostomy on the table and the other of prolonged loss of pancreatic juices. The other seven patients recovered.

Prognosis

Twenty-six patients died. The chance of any particular patient dying seemed to depend more on the severity of the attack and the resistance of the patient than on the treatment employed. Some of the factors involved were as follows:

Age.—Of 26 patients below the age of 50, only four died (15%). From 50 to 60 the fatality rate was 22%, from 60 to 70 it was 29%, and over the age of 70 it was 40%.

Sex.—Seven men and nineteen women died.

Severity of Attack.—It is difficult to measure this. The significance of a lowered serum calcium and of the development of diabetes has been mentioned. Apart from these, and the evil significance of uraemia and hypoproteinaemia, it is difficult to prognosticate in the individual patient. Certainly the level of amylase activity in the blood does not reflect the outlook, but a prolongation of the elevation of serum amylase means continued activity of the disease and carries a higher mortality rate. There were 19 patients whose serum amylase was estimated daily and fell to normal within five days. Two of them died (10%). On the other hand, among 30 patients whose serum amylase remained elevated for more than five days, 7 died (23%).

Provided no heroic surgery is undertaken, immediate operation has no deleterious effect on survival. Thirty patients in this series were operated on during the first week of their illness. There were six deaths (20%). Five patients were moribund and died within 24 hours. Of the 65 patients deliberately treated conservatively, 15 died (23%).

A great many patients recover from an attack of acute pancreatitis completely and have had no further trouble, or only mild indigestion, during the one to five years that they have been followed. On the other hand, no fewer than 25 patients gave a history of previous similar attacks, in five of whom a diagnosis of acute pancreatitis was proved at laparotomy. Of the 74 surviving patients, 13 (17%) have had subsequent similar attacks; in 6 of them the diagnosis was proved at laparotomy or by gross elevation of the serum amylase level.

There were thus 11 patients who have had at least two proved attacks of pancreatitis. Of these patients, two died during their second attack, one has recovered from his second attack very recently, four are in good health from one to four years after their second attack, and four have been subjected to transduodenal sphincterotomy, with one death and three satisfactory results up to 18 months.

The high percentage of patients who recover from acute pancreatitis and have no further attacks is striking. It is in line with findings in other published series—for example, Rake and Bartlett (1953). The liability to recurrent attacks does not seem to depend on initial or subsequent treatment.

Treatment

The basic principles of management of patients with acute pancreatitis are well known and are not controversial. They are: resuscitation, control of superadded infection by antibiotics, and control of metabolic and electrolyte disturbances. About other aspects of treatment there is considerably more dispute. These include antispasmodics, antitryptic substances, corticoids, and finally operations.

Resuscitation.—In a severe case of acute pancreatitis the circulating blood volume is suddenly and dramatically reduced and the patient shows clinical signs of shock. Elliot, Zollingen, Moore, and Ellison (1955) have shown a profound fall in circulating blood volume after the experimental induction of pancreatitis in dogs and that the mortality can be reduced by the generous intravenous administration of serum albumin. Fifteen of our patients have been treated by immediate intravenous infusions of 1–3 litres of blood or plasma, and a further 11 by immediate intravenous infusion of electrolyte solutions. Thirteen of these 26 seriously ill patients died, but only three died within five days of the onset of their illness. Shock has given place to later complications as an important cause of death in pancreatitis.

Antibiotics.—It is customary to treat these patients with penicillin or other antibiotics. Seventy patients in the present series have been so treated, with results that are on the whole disappointing. Certainly the incidence of septic complications is less, but many of these patients still die of uncontrollable metabolic and electrolyte disturbances. Comparisons within this series are valueless, since it has been our policy for many years to treat all severe cases of pancreatitis with antibiotics.

Control of Metabolic and Electrolyte Disturbances.—Seventeen patients in the present series either had been or became diabetic. The control of the diabetes with soluble insulin has presented no problems, but one death can possibly be ascribed to untreated diabetic coma. Electrolyte disturbances are common in the more severe forms of the disease, and their correction may prove impossible. Sodium, potassium, and chloride deficiencies have been found, together with acidosis or alkalosis, and correction has been attempted by the usual measures of oral, rectal, and intravenous replacement. It has already been mentioned that tetany may occur, associated with a depression of the serum calcium level. This has been found difficult to correct, and every patient with this complication has died. Hypoproteinaemia and anaemia are commonly found in the later stages of acute pancreatitis and have been treated by blood transfusions.

The main problem with severe cases, however, has been their catastrophic katabolism. In a few patients accurate estimation of the rate of weight loss was possible, and it was found to approach a kilogram a day. This process we have found impossible to control, and most of these patients have died. In the few who have survived, no particular treatment appeared to mark the turning-point. We have had no experience of the use in this condition of androgenic steroid hormones, but have been very disappointed with the results of blood transfusions, high-protein forced feeding, and corticoids.

Antispasmodics.—The assessment of the place of atropine and other drugs with similar action is difficult. In this series atropine or propantheline (pro-banthine) has been used in 12 patients without noticeable effect

on the course of their illness. Theoretically morphine, a potent cause of spasm of the sphincter of Oddi and of the duodenal wall, should not be used in this disease, and in fact most patients who needed analgesics were treated with pethidine.

Antitryptic Substances.—It is likely that some of the general and local effects of acute pancreatitis are due to the liberation of large quantities of active trypsin from the damaged pancreas. There are known to be several substances with high antitryptic potency, and the use of these substances might appear to be indicated in this disease. Evidence from experimental sources (Elliott *et al.*, 1955; Pollock, 1956) indicates that their value is strictly limited. For two years in this hospital it was customary to transfuse large quantities of plasma on account of its albumin content (human serum albumin has been shown *in vitro* to be a potent trypsin inhibitor). No effect has been detected from this treatment, apart, as indicated earlier, from its beneficial effect on shock. Five of the 15 patients so treated died. The most potent trypsin inhibitor has been isolated from soya beans (Kunitz, 1947). This substance has not been tried clinically, but it has been found not to influence the course of experimental pancreatitis (Elliott *et al.*, 1955).

Corticoids.—The first report of the treatment of acute pancreatitis by corticoids seems to be by Stephenson, Pfeffer, and Saypol (1952). Since then isolated cases and small series have been reported, all of which have claimed good recoveries after their use—for example, Rogers, Wilson, Meynell, and Cooke (1956). There has at the same time grown up a volume of experimental and clinical evidence that cortisone may cause pancreatitis. Thus Stumpf, Wilens, and Somoza (1956) found pancreatitis in rabbits treated with cortisone, and Baar and Wolff (1957) reported two fatal cases of acute pancreatitis in children treated with cortisone. In order to elucidate this question, a "double blind" controlled trial of corticotrophin in pancreatitis is at present being conducted. Thirty patients have so far been treated by either corticotrophin or an inert substance resembling corticotrophin in a dose of 40 units twice daily, reducing after 10 days and being stopped after 14 days. The results are being analysed by the restricted sequential procedure of Armitage (see Snell and Armitage, 1957). It is planned to treat 50 patients, but the preliminary results indicate no clear superiority of corticotrophin over placebo.

In one patient laparotomy was performed after the patient had been receiving twice-daily injections of 40 units of corticotrophin for 10 days. Apart from the acute pancreatitis which was confirmed, he was also found to have a recently perforated and sealed acute duodenal ulcer. This may be attributable to the action of the corticotrophin.

Operations

It has become generally accepted that immediate operation in patients with pancreatitis can do no good, and that elective surgery should await the subsidence of the acute attack. On the other hand, diagnostic laparotomy has not been shown to do any harm, and in any doubtful case it is preferable to make sure of the diagnosis by laparotomy rather than miss another condition mimicking it and associated perhaps with an elevated serum amylase level.

When a mass becomes palpable there may be a temptation to explore it with a view to drainage. This should be resisted for two reasons: first, some masses resolve spontaneously; second, external drainage of a recent pseudo-pancreatic cyst invites the occurrence of a pancreatic fistula with its accompanying loss of electrolytes and protein. Provided the patient's general condition is reasonably satisfactory, it is far better to wait for six to eight weeks before operating on a pseudo-pancreatic cyst. By that time it will have become well walled off and may be drained externally or internally with little fear of doing more harm than good. Our own feeling in recent years has been in favour of transgastric anastomosis of the anterior cyst wall to the posterior stomach wall. This simple operation has proved effective in five patients recently. Barium-meal *x*-ray studies have shown no trace of the cysto-gastrostomy after as short a period as one week. Apparently the cyst, having discharged into the stomach, does not fill up again with gastric contents.

The treatment of a diseased gall-bladder after an attack of pancreatitis is more controversial. The traditional view is that the gall-bladder should be removed and that the common duct should be explored if it is dilated. There is, however, a certain amount of theoretical and experimental evidence that after cholecystectomy (or if the gall-bladder is not functioning), the pressure in the common duct may exceed that in the pancreatic duct and result in bile reflux and recurrent attacks of pancreatitis. Certainly in the present series cholecystectomy has not been found to protect the patient against attacks of pancreatitis. Four patients have had recurrent attacks of pancreatitis following cholecystectomy.

In three patients after an attack of pancreatitis the gall-bladder was anastomosed to the stomach. Two of these have had recurrent attacks of pancreatitis, while the third has remained well for five years.

Prolonged T-tube drainage of the common bile duct was used in one patient, who remained well two years later.

Transduodenal Sphincterotomy.—This operation has been used in one patient during her first attack of acute pancreatitis (she suffered a disruption of her duodenal incision and subsequently died of an acute enterocolitis), and in five patients with recurrent acute pancreatitis. One of these five died of a fulminating attack of acute pancreatitis four days later. The remaining four have remained well for 6 to 18 months. The operation is technically easy and theoretically satisfying. It remains to be seen whether the late results justify its continued use. Doubilet and Mulholland (1956) claim that they do.

Finally, it should again be stressed that the great majority of patients who recover from an attack of pancreatitis suffer very few after-effects and that recurrent pancreatitis is a rare disease.

Summary and Conclusions

A series of 100 patients with acute pancreatitis have been studied and reviewed after periods of up to five years.

In half the men and three-quarters of the women in this series the gall-bladder was abnormal. In the presence of a non-functioning gall-bladder the pressure of bile in the common duct may be raised above the pressure in the pancreatic duct. If the ampulla is common to both ducts and if a functional or organic obstruction at the sphincter of Oddi occurs bile may

be forced up the pancreatic duct to initiate an attack of acute pancreatitis.

The general and local effects of pancreatitis are due primarily to the liberation into surrounding tissues and the blood stream of large quantities of active pancreatic enzymes.

Electrocardiographic changes suggestive of myocardial infarction may occur in acute pancreatitis. On the other hand, two patients with myocardial infarction have been seen with grossly elevated serum amylase levels (above 600 units, Somogyi).

Radiographic changes in pancreatitis are discussed. Barium-meal examination early in the course of the disease may prove to be of diagnostic value.

A serum amylase level of over three times the normal (200 units, Somogyi's method) has been found in association with a few cases of perforated gastric ulcer, intestinal obstruction, gall-stones, ruptured ovarian cyst, and myocardial infarction.

Local and general complications are discussed. Six patients developed clinical tetany, and they all died.

One-quarter of all the patients in this series died. Some of the factors influencing prognosis are discussed.

Treatment is discussed in terms of resuscitation, antibiotics, control of electrolyte and metabolic disturbances, antispasmodics, antitryptic substances, corticoids, and operations. A mild case of pancreatitis will recover whatever treatment is given, and for a very severe attack no treatment appears to be of any avail. Most patients who recover from an attack of acute pancreatitis have remained well for one to five years.

I am grateful to all the surgeons, physicians, and pathologists of the General Infirmary at Leeds who have over the past five years allowed me to see their cases. In the present series are patients admitted under the care of Messrs. Armitage, Chamberlain, Latchmore, Oldfield, Shucksmith, and Symons, and of Professors Goligher, Moir, Pyrah, and Tunbridge.

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ELECTROLYTE LOSSES ASSOCIATED WITH THE TAKING OF PURGES INVESTIGATED WITH AID OF SODIUM AND POTASSIUM RADIOISOTOPES*

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It is well known that diarrhoea may result in excessive loss of electrolytes from the bowel, and if the intake is not large enough to keep the patient in balance body depletion will occur.

There are reports that continual purging produces abnormal loss of electrolytes through diarrhoea (Mårtensson, 1953; Schwartz and Relman, 1953; French *et al.*, 1956; Houghton and Pears, 1958; Aitchison, 1958). In this paper three cases are described in which the regular taking of purges was partly or wholly responsible for excessive loss in the stools of sodium or potassium, or both, and for depletion of the body stores of these substances. Electrolyte studies were made in these patients, using chemical balances and radioisotope methods to be described elsewhere (Lubran, 1959).

Case 1

A woman aged 50 was referred in October, 1953, for gastro-intestinal investigation. She had been constipated since early childhood. At 5 years of age rectal prolapse occurred, and from that time she took purges. Without them her bowels did not move and abdominal distension developed. From the age of 20 she had taken the same laxative‡ daily. At 40 years of age diarrhoea with colicky pains began and she passed eight to ten loose stools daily. Even so, she found it impossible to stop taking her customary nine laxative tablets daily, for without them, although continuing to pass about six liquid stools in the day, she was unable to pass sufficient flatus and her abdomen became uncomfortably distended. In November, 1952, ammonium urate stones were removed (by Mr. J. Scholefield) from the left renal pelvis. In March, 1953, she first noticed blood and mucus in the stools.

First Admission (October 23, 1953)

On examination the abdomen was distended, and tender in both iliac fossae. No abnormality was found in any other system.

Investigations.—Stools contained pus and red blood cells but no pathogenic organisms or parasites. Sigmoidoscopy showed a reddened mucosa with superficial ulceration compatible with moderately severe ulcerative colitis. A plain

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†In receipt of a grant from the Research Fund of the North-West Metropolitan Regional Hospital Board.
‡Composition:

Comp. ext. of colocynth, *B.P.*, 1914	1 gr. (60 mg.)
Ext. of jalap	½ gr. (30 mg.)
Podophyllum resin	¼ gr. (15 mg.)
Green ext. of hyoscyamus, *B.P.*, 1898	¼ gr. (15 mg.)
Menthol	1/20 gr. (3 mg.)

x-ray film of the abdomen revealed a colon very distended with gas, and a barium enema showed it to be shortened, with absent haustrations and irregular in outline. The ileum was irregular and narrowed in its last part. Examination by barium meal showed a normal small intestine except for the same changes in the terminal 6 in. (15 cm.) of the ileum. The serum contained (in mEq/l.) sodium 140, potassium 4.6, chloride 90, calcium 4.6, and phosphate 2.2. The stools contained 4.3 g. of fat daily over six days on a daily intake of 55 g. of fat (92% absorption).

Progress.—The temperature was variably raised to 100° F. (37.8° C.). The patient was allowed her nine laxative tablets nightly and six to ten stools were passed daily. It was noted that she had a craving for sour foods and salt, and she revealed that for many years she had sucked two to four raw lemons daily, having first dipped the cut surfaces in table salt. It was estimated that her total daily intake had been about 730 mEq of sodium and 36 mEq of potassium. When she was discharged home she was asked to reduce the laxative tablets to five nightly. During the next two weeks the stools fell to about six daily, but abdominal discomfort and distension developed. Then the tablets were reduced to three nightly, but the abdominal discomfort became unbearable, and she had to return to a dose of five or six tablets. By January, 1954, the stools had increased to 12 daily and contained large amounts of blood and mucus.

Second Admission (March 1, 1954)

Physical examination and sigmoidoscopic appearances were unchanged. Observations were made with the patient taking purges and after she had stopped them (Fig. 1). Without the purges the stools diminished in frequency and weight; they became semi-formed and blood and mucus disappeared. The craving for salt and lemons lessened. The body weight rapidly increased, and was associated with the development of oedema of ankles and sacrum. When, because of increasing abdominal discomfort, a single dose of four tablets was given, the patient began within a few hours to pass numerous liquid stools containing blood and mucus. Because of the profuse diarrhoea some of the stools were lost and output could not be measured on that day. The body weight fell by 3.9 kg. in 24 hours and the oedema lessened. A further single dose of one tablet also resulted in frequent stools and loss of 1.5 kg. in weight.

Radioisotope Studies (Table I) and Chemical Balance (Fig. 1).—A radiosodium test (March 30), when the patient was taking purges showed a low sodium space and a low exchangeable sodium, indicating depletion of body water and sodium. Radiosodium did not appear in the urine, but there were large amounts (18.5% of the dose) in the stools. On the same dose of purge a chemical balance (April 6 to 14) confirmed the very low urinary and the very high faecal excretion of sodium. Except for one day, the balance was always positive owing to the high intake of sodium. After the purge was stopped (April 21) the chemical balance showed an increased sodium content in the urine and a marked decrease in the stools. Even on a lower intake the balance remained positive owing to the reduced faecal loss. The radiosodium test, repeated three weeks after the purges had been stopped (except for the single dose of four tablets), revealed that the sodium space had become normal and the exchangeable sodium high. These changes coincided with the oedema due to sodium retention. The urine now contained a good amount of the dose (17.2%) and the faeces a smaller but still abnormal amount (4.8%).

TABLE I.—*Intravenous ^{24}Na Studies in Case 1*

	4-hour Sodium Space* (ml./kg.)	24-hour Exchangeable Sodium† (mEq/kg.)	48-hour Urinary Excretion (% of Dose)	48-hour Faecal Excretion (% of Dose)	Serum Sodium (mEq/l.)
Normal value (mean) (s.d.)	276‡ (29)	39·5§ (2·3)	—‖	0·12‡ (0·16)	144 (3·6)
Taking purges (March 30, 1954)	222¶	35·9	0	18·5	136
Off purges (May 11, 1954)	271	47·7	17·2	4·8	133

* Sodium space: The volume of body fluid in which administered radioactive sodium is distributed in a given time (usually four hours). This is approximately equal to the extracellular fluid volume.
† Exchangeable sodium: The weight of body sodium in which the administered radioactive sodium is distributed when equilibrium between radioactive and non-radioactive sodium has been established (usually 24 hours). This is approximately the body content of sodium.
‡ Coghill *et al.* (1956). Lubran (1959).
§ For females (Forbes and Perley, 1951).
‖ In normal subjects the percentage of the dose of ^{24}Na excreted in the urine varies considerably and is largely determined by the dietary intake of sodium.
¶ Two-hour space.

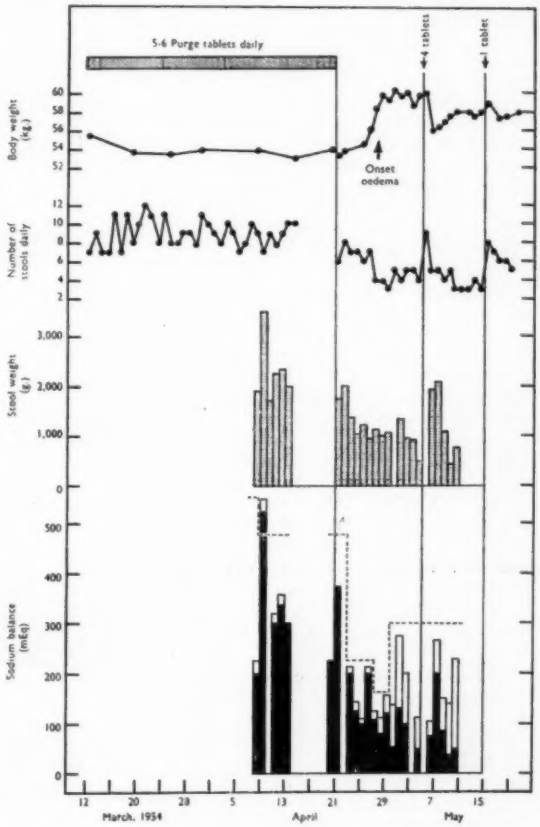

FIG. 1.—Case 1. In the electrolyte balance the black columns represent the electrolyte content of faeces and the unshaded columns the electrolyte content of urine. The intake is at the level of the interrupted line, and the output is plotted upwards from zero. When the columns extend above the interrupted line the balance is negative. Where there is no entry in the balance it is because no collections were made or completed that day. The normal value for faecal content of sodium is less than 10 mEq each 24 hours (Bodansky and Bodansky, 1952). The urine collection was lost on April 14, 21, and 22.

Fat Absorption.—During the same period of study the daily fat content of the stools was estimated (daily fat intake 55 g.). The results were normal except for four occasions while she was on purges, when the fat excretion was increased to around 8 g. daily (upper normal limit 7 g. each day; French, 1955). The lowest level of absorption was 80%. An oral glucose-tolerance test at this time was normal.

Further Progress.—Although the diarrhoea decreased when the purges were stopped, abdominal pain and distension increased. As her colon was severely diseased colectomy seemed the only solution to this impasse. A subtotal colectomy was performed (Mr. J. Scholefield), with the

establishment of an ileostomy. The mucosa of the terminal ileum and colon was oedematous, inflamed, and ulcerated. The rectum was removed at a later operation. Subsequently the patient has remained well and has not taken further purges.

Comment

The continual purgation aggravated the ulcerative colitis and clearly increased the frequency and bulk of the liquid stools. Large amounts of sodium were thus lost from the bowel, producing a low sodium state. The purging also resulted in water depletion (predisposing to renal stones).

Case 2

An unmarried woman aged 39 was referred in July, 1953, for investigation of intermittent diarrhoea. Since 1946 she had had bouts of abdominal pain and diarrhoea with up to eight fluid stools daily containing mucus but no blood. In 1947 the gastro-intestinal tract had been thoroughly investigated (including laparotomy) with negative results.

Physical examination in July, 1953, revealed mild tenderness in the hypogastrium and right iliac fossa. No abnormality was present in any other system. At sigmoidoscopy the anal canal was inflamed and bled easily, but the rectum and colon were normal. The stools contained undigested food. Barium-meal and enema examinations were normal. The serum contained (in mEq/l.) sodium 145, potassium 5.2, and chlorides 98. The daily dietary intake was estimated to be 285 mEq of sodium and 64 mEq of potassium.

Progress (July, 1953, to February, 1955)

Abdominal pain and diarrhoea continued unchanged. A sensation that the rectum and vagina were sore and "on fire" developed. Mr. D. A. Davies could find no gynaecological cause for these new symptoms. Laboratory and radiological investigations of the gut, repeated a number of times, never revealed any abnormality. However, serial sigmoidoscopies from July, 1954, onwards showed moderate oedema and reddening and granularity of the mucosa, which appeared first in the rectum and later progressed up the colon for 26 cm. The stools at this stage contained more mucus and also some blood.

Attempts at therapy with opium, kaolin, belladonna, propantheline, or hexamethonium, although partially effective in reducing the stool frequency, were often objected to by the patient on the grounds of side-effects. Dr. F. P. Haldane found anxiety and hostility to psychiatric investigation. The patient was of mediocre intelligence, with obsessional and paranoid tendencies.

Radiosodium Studies (Table II).—An intravenous test on July 20, 1954, showed a reduced sodium space and a low exchangeable sodium, indicating dehydration and depletion of sodium. An abnormally large amount (7.4%) of the injected dose of radiosodium appeared in the stools. The test was repeated on November 16, and showed that the sodium space and exchangeable sodium were now within normal limits. Nevertheless the faecal excretion was still high (8.2%), suggesting that excessive faecal loss of sodium had persisted. Three further tests (intravenous and oral) in January and February showed low values once more for the sodium space and exchangeable sodium and a continued high rate of faecal excretion. There was an abnormally high loss of sodium in the stools also in the oral tests of November 23 and February 8, 1955.

Chemical Balances (Fig. 2).—During the period January 13 to 30, 1955, there was a nearly constant positive balance of sodium, but sometimes a slightly negative balance of potassium. The high faecal excretion of sodium found in the radiosodium tests was confirmed in the chemical balances. The faecal loss of potassium was also higher than normal. During the chemical processing of stools for fat estimations for balance studies it was unexpectedly observed that phenolphthalein was present in all specimens. A similar accidental finding occurred in the case reported by French *et al.* (1956), who used the same technique for faecal fat estimations (van de Kamer *et al.*, 1949). It was noted also that in the radiosodium tests the greatest number of stools were passed during the eight-hour period of 2 to 10 a.m. (Table III), and that these usually contained three or four times more sodium than the stools passed in either of the two earlier periods. It is during these hours that a purge taken the previous evening might be expected to exert its main effect. When taxed the patient reluctantly admitted

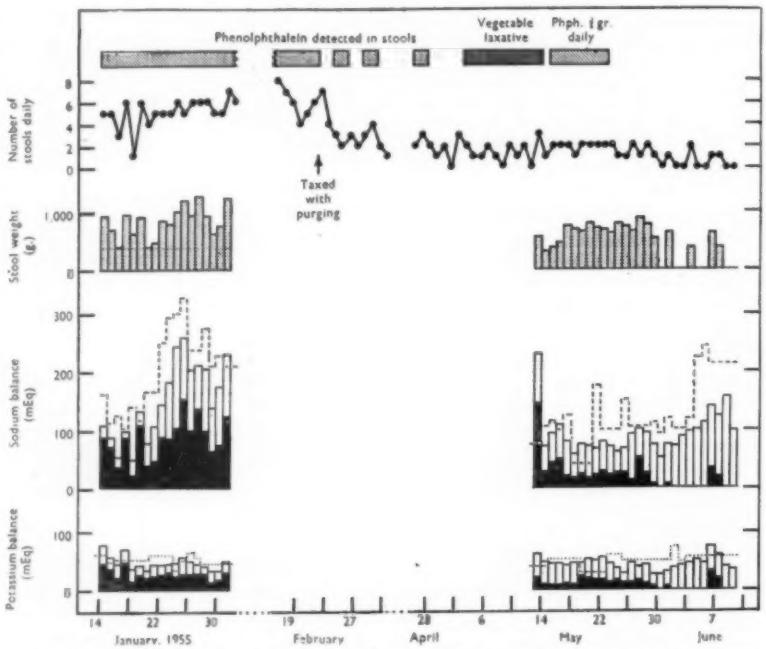

FIG. 2.—Case 2. The balances are arranged as in Fig. 1. The normal value for faecal content of potassium is less than 10 mEq each 24 hours (Bodansky and Bodansky, 1952). Phph = Phenolphthalein.

TABLE II.—*Radiosodium Studies in Case 2*

Date	Route of Dose	4-hour Sodium Space (ml./kg.)	24-hour Exchangeable Sodium (mEq/kg.)	48-hour Urinary Excretion (% of Dose)	48-hour Faecal Excretion (% of Dose)	Serum Sodium (mEq/l.)
20/7/54	I.V.	181	33·2	2·6	7·4	155
16/11/54	,,	324	43·1	4·4	8·2	139
23/11/54	Oral	253	—	1·2	4·5*	147
11/1/55	I.V.	197	28·4	4·0	8·7	130
1/2/55	,,	256	36·8	5·7	7·4	133
8/2/55	Oral	195	28·0	5·9	9·1	128
19/4/55	I.V.	360	55·0	7·3	0·1	142
17/5/55	,,	292	41·7	5·4	0·5	134
10/6/55	,,	294	45·5	3·1	0·0	144

Oral and intravenous routes give essentially the same sodium space (Miller and Wilson, 1953).
* First two stools discarded in error.

TABLE III.—*Case 2. Further Details of Radiosodium Tests in Table* II (*July* 20, 1954, *to February* 8, 1955, *Inclusive*)

8-hour Periods (First 24 Hours)	No. of Stools						Percentage of Dose in Stools					
10 a.m.–6 p.m.	1	2	2	2	2	1	0·9	1·4	?	0·1	1·4	0
6 p.m.–2 a.m.	?	0	0	?	0	2	0·9	—	—	1·3	—	2·9
2 a.m.–10 a.m.	2	4	2	5	4	4	2·8	4·4	1·8	5·1	4·0	3·9
Totals for 48-hour period	8	12	8	11	11	10	7·4	8·2	4·5	8·7	7·4	9·1

that she took purges when constipated and for relief of rectal discomfort. She never confessed the full extent to which she had evidently indulged in the practice, nor would she say what particular preparation she used.

Further Progress (April to June, 1955)

During a later period of in-patient observation it was noted that stool frequency had fallen to once or twice daily (Fig. 2). Sigmoidoscopy showed that the mucosa of the colon and rectum had returned to normal. Phenolphthalein was still found intermittently in the stools, so it was evident that the patient had not renounced purges completely but was probably taking smaller quantities. She was given a vegetable laxative and was asked not to take her own purge. After this phenolphthalein disappeared from the stools. The new purge* contained no phenolphthalein and was given daily for eleven days, and throughout this period phenolphthalein remained absent from the stools. After this, unknown to her, phenolphthalein ¼ gr. (45 mg.) daily was incorporated in her food and was easily detectable in the stools. The frequency and weight of the stools were not appreciably increased by either of these purges, but after they were stopped the patient became constipated.

Radiosodium Studies (Table II).—Intravenous tests were repeated while the smaller doses of purges were being taken (April 19 and May 17), and again after the purges were stopped (June 10, 1955). All tests showed normal values for sodium space and exchangeable sodium. Also, the faecal excretion of sodium had become much smaller and was now usually within normal limits.

Chemical Balance (Fig. 2).—Further estimations showed that there was an almost constant retention of sodium and potassium between May 13 and June 9, 1955, and this was greatest when the purges were stopped and the stools were reduced in number. The amount of sodium and potassium in the faeces became low and mostly within normal when the purges were reduced or stopped.

Fat Absorption.—Whilst the vegetable laxative or the small dose of phenolphthalein was being taken the daily fat content of stools was within normal limits except for an increase on two occasions to around 8 g. (daily fat intake 115 g.).

Comment

The diarrhoea in this case seemed by all evidence to be related to the taking of large doses of phenolphthalein in secret. They were taken to relieve doubtful constipation and unpleasant rectal symptoms which were probably related to her abnormal mental state. Excessive loss of sodium and potassium in the faeces was produced constantly by the purging, and usually was associated with low stores of sodium and water.

Case 3

A married woman aged 68 was admitted to hospital on January 19, 1956, with a history of increasing weakness of the limbs for four months, and inability to walk for nine days. Five years previously her blood pressure had been found raised, and since that time her daily salt intake had been restricted to about 40 mEq of sodium and 34 mEq of potassium. For 40 years she had thought she suffered from constipation and had taken a regular nightly laxative* which resulted in three or four liquid stools every day.

Physical Examination.—She was ill and apathetic, with arms completely paralysed except for ability to lift the right arm just off the bed. Her legs were also paralysed, but slight movement was retained at the ankle-joints. The limbs were flaccid, and reflexes were absent except for the ankle-jerks. No abnormality was present in any other system. Blood pressure was 140/90 mm. Hg. A clinical diagnosis of potassium deficiency was made.

Investigations.—The serum contained potassium 1.8, sodium 139, and calcium 4.5 mEq/l., 98 vols CO_2/100 ml., and urea 25 mg./100 ml. An electrocardiogram showed abnormalities compatible with hypokalaemia (depressed ST segments and flat T waves). The first specimen of urine passed on the day of admission before treatment contained 18.0 mEq of potassium per litre and 33.1 mEq of sodium per litre. The urine passed during the next 24 hours contained 6.9 mEq of potassium and 18.3 mEq of sodium. The Van Slyke urea clearance test showed a standard clearance of 130% of the average value. Sigmoidoscopy revealed normal appearances except for an extreme degree of melanosis coli.

Progress

The potassium deficiency was treated at once to avoid the possibility of myocardial damage (McAllen, 1955). After 12 hours' treatment with potassium (100 mEq intravenously and 40 mEq orally) and sodium (350 mEq intravenously) slight but definite improvement occurred in muscle power. At this time the serum contained potassium 2.4, sodium 139, and chlorides 85 mEq/l. The alkali reserve was unchanged.

TABLE IV.—*Intravenous Radiopotassium Tests in Case* 3

Date	24-hour Exchangeable Potassium* (mEq/kg.)	24-hour Urinary Excretion (% of Dose)	24-hour Faecal Excretion (% of Dose)	Serum Potassium (mEq/l.)
Normal value (Mean and range)	40·7† (28·6–47·2)	—‡	0·48 (0–1·3)	4·52 (s.d. 0·45)
25/1/56	32·2	0·34	0·01	7·0
30/1/56	Started purges: one pill every evening			
7/2/56	32·8	0·62	0·60	4·5
10/2/56	One-half purge pill every evening up to and including Feb. 17			
15/2/56	37·1	1·91	0·68	—
13/3/56	39·1	1·83	0·23	3·9

* Exchangeable potassium. The weight of body potassium in which the administered radioactive potassium is distributed when equilibrium between radioactive and non-radioactive potassium has been established (usually 24 hours). This is approximately the body content of potassium.
† Edelman *et al.* (1952), for females.
‡ In normal subjects the percentage of dose of potassium excreted in the urine is variable and is largely determined by the intake of potassium.
§ Lubran (1959).

TABLE V.—*Intravenous Radiosodium Tests in Case* 3

Date	4-hour Sodium Space (ml./kg.)	24-hour Exchangeable Sodium (mEq/kg.)	48-hour Urinary Excretion (% of Dose)	48-hour Faecal Excretion (% of Dose)	Serum Sodium (mEq/l.)
27/1/56	203*	32·3	5·56	0·17	136
30/1/56	Started purges: one pill every evening				
3/2/56	310	48·8	1·20	0·70	134
10/2/56	One-half purge pill every evening up to and including Feb. 17				
18/2/56	298	40·7	30·0	1·15	137

* Three-hour space.

After five days' treatment (total potassium 1,090 mEq, total sodium 920 mEq) all four limbs could be moved well and all limb reflexes had returned. The blood pressure rose to 160/100 mm. Hg and the electrocardiogram became normal. As the serum potassium had risen to 7.4 mEq/l. all electrolyte therapy was stopped and a normal diet started.

Radioisotope Studies (Tables IV and V) and Chemical Balance (Fig. 3).—A radiopotassium test carried out two

*Composition:
Ext. colocynth co. .. .. .. 1 gr. (60 mg.)
Jalap resin .. .. ¼ gr. (15 mg.)
Podophyllum resin .. .. .. ¼ gr. (15 mg.)
Hyoscyamus sicca .. .. .. ¼ gr. (15 mg.)
Peppermint oil .. .. 1/10 min. (0.006 ml.)

*Composition:
Aloin .. .. 2 gr. (120 mg.)
Ext. belladonna sicca .. .. .. ¼ gr. (15 mg.)
Ext. nuc. vom. sicca .. .. .. ½ gr. (30 mg.)

days after electrolyte therapy was stopped (January 25) showed that the exchangeable potassium was low and indicated that potassium lack was not yet fully corrected in spite of the high serum potassium level. A radiosodium test performed soon afterwards (January 27) showed a low sodium space and a low exchangeable sodium, revealing mild dehydration and lack of sodium. The daily stool weight and the chemical content of potassium and sodium were estimated and then the effect of restarting the laxative was noted. There was a quick rise in the stool frequency, weight, and chemical content of potassium and sodium. After eight days' purgation the exchangeable potassium was again low and the faecal content of radio-potassium and radiosodium was a little increased. The patient became frightened by the diarrhoea, and the purge had to be reduced and then stopped. Thereafter the stools dropped to one a day. Radioisotope studies performed after stopping the purges revealed normal values for exchangeable potassium, exchangeable sodium, sodium space, and sodium content of stools.

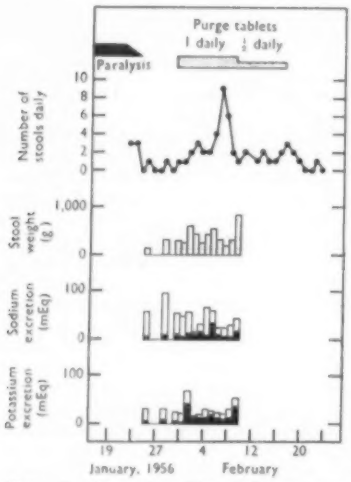

FIG. 3.—Case 3. The balances are arranged as in Figs. 1 and 2.

Comment

Renal disease, causing abnormal urinary loss of potassium, was excluded by the low level of urinary potassium on admission and by the normal renal function tests. The low potassium state was mainly due to loss of potassium in the liquid faeces. There was no evidence of bowel disease, and the diarrhoea was apparently due to regular purgation. When the purge was restarted diarrhoea returned, resulting in increased faecal loss of potassium (and sodium).

Discussion

Constipation is the usual explanation for the frequent taking of purges. The first patient took purges for 35 years for this reason, and when ulcerative colitis developed she continued taking them to relieve the discomfort of the associated abdominal distension. It is doubtful if the second patient was more than mildly constipated, but for about seven years she desired a purge to relieve rectal symptoms of obscure origin. In Case 3 constipation was the only cause for 40 years of purge-taking. Diarrhoea resulted from the purges in Cases 2 and 3 and was made worse in Case 1. Excessive loss of sodium and potassium occurred in the stools and produced varying degrees of depletion of the body stores of these substances. (The potassium state was not studied in Case 1.)

The dietary intake of electrolytes must be reduced to some critical level before an abnormal loss will produce clinical effects of deficiency. In Case 1 the large faecal loss of sodium was compensated over many years by the very high dietary intake (730 mEq daily). In Case 2 the moderate loss of sodium and potassium was balanced by an adequate diet. In Case 3 slightly excessive amounts of potassium were lost in the stools, and no doubt the diet covered this until the last five years of purge-taking, when the intake became low. Even so, the hypokalaemic paralysis did not occur until the end of these five years. It may be, as Schwartz and Relman (1953) have suggested, that muscles can become acclimatized to potassium deprivation when it is very slowly induced.

Information about the pharmacological action of "irritant" purges on the small and large intestine is surprisingly scanty and conflicting. The drugs colocynth, jalap, podophyllum, and aloin are purges which are classed as irritants, being said to act mainly on the large intestine, causing increase of motility (Goodman and Gilman, 1955). Phenolphthalein, in spite of being commonly classed as an irritant, probably acts by direct stimulation of the muscle of the large intestine, with the same effect (Blick *et al.*, 1942). The hurry of the contents of the large intestine caused by these drugs may interfere with the completion of sodium absorption which takes place in that organ, and sodium may be lost excessively in the stools. Little is known about the absorption of potassium from the normal colon. Work on patients with uretero-sigmoidostomies suggests that under these conditions the colon absorbs little of it (Parsons *et al.*, 1952; Annis and Alexander, 1952). Dietary potassium is probably mainly absorbed in the ileum, and when excessive quantities appear in the stools in the absence of bowel disease it suggests small-intestinal hurry. There is some evidence that colocynth (Magnus, 1909; Padtberg, 1910; Gruber *et al.*, 1932), jalap (Bloch, 1937), and podophyllum (Gruber *et al.*, 1932) may increase the motility of the small as well as the large intestine, at least in animals. As regards aloes very little information, and that contradictory, is available about its site of action (Meyer-Betz and Gebhardt, 1912; Lenz, 1932).

In Cases 1 and 2 the occasional steatorrhoea and the presence of undigested food in the faeces would be difficult to explain except on the basis of small-intestinal hurry due to the purges. Steatorrhoea has been described in association with right-sided ileocolitis by Cooke and Brooke (1955); but the mild steatorrhoea in Case 1 ceased when the purges were stopped, and this suggested that it was related to the purging rather than to her ileocolitis. Mild steatorrhoea was also found in one of the two cases of diarrhoea due to taking purges described by French *et al.* (1956), and this was attributed to an effect of phenolphthalein on the small intestine. However, the evidence is against this particular drug having an action on the small intestine (Caldwell and Crane, 1929; Blick *et al.*, 1942), and their patient may have taken a mixed laxative preparation containing other drugs. For example, in our Case 2 it was impossible to know whether purges other than phenolphthalein were also taken.

It is of interest to consider if the purges could have caused the ulcerative colitis in Case 1 or the proctosigmoiditis in Case 2. Irritant purges are taken widely, and it is difficult to believe that in their usual small dosage they can produce inflammatory changes in the gut. However, it is said that colocynth and jalap in large doses may cause inflammation of the intestine (Grollman and Slaughter, 1947). In Case 1 unusually large doses of these purges were taken, but if they played any part in the ulcerative colitis they took at least 20 years to do so. Heilbrun (1943) described the

case of a patient who took large doses of phenolphthalein, aloin, and podophyllum for 20 years and developed ileocolitis in many respects similar to that in Case 1. Heilbrun's patient and one other (Jewell and Kline, 1954) showed radiological evidence of improvement of the colon when the purges were reduced or stopped. However, it is most unlikely that the severe colitis in Case 1 would have healed even if it had been possible to stop the purges. Further, aloin was taken by Case 3 for 40 years without colitis arising; and, again, the two patients reported by Schwartz and Relman (1953) also took irritant purges with resultant severe loss of potassium but did not develop signs of colitis. In Case 2, when the purge was reduced the proctosigmoiditis disappeared, and here it is conceivable that the purge was the cause of the bowel changes.

Summary

Three cases are described in which chronic purgation caused excessive loss of sodium, potassium, and water in the faeces and gave rise to electrolyte-deficiency states. These disturbances were studied by chemical and radioisotope methods.

The manner in which these losses were brought about is discussed and the inadequate knowledge of the action of common purges on the intestine noted. The evidence in these cases suggested that "irritant" purges may exert an action on the small intestine.

This work was done in collaboration with Dr. M. Lubran, who was responsible for the laboratory investigations and who is publishing elsewhere (Lubran, 1959) an account of the methods used, with results in normal controls. We are grateful to Mr. J. Scholefield for referring these patients to us and for his help and co-operation in the studies undertaken in Case 1. We also thank Miss E. R. Harrison, lately senior dietitian at the hospital, for the diet histories; and Miss S. M. Robinson for help with the charts.

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PLEUROPNEUMONIA-LIKE ORGANISMS IN GENITAL INFECTIONS*

BY

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In his monograph on non-gonococcal urethritis Harkness (1950, p. 1) says of the pleuropneumonia-like organisms (P.P.L.O.) that "their frequent association with certain types of abacterial urethritis forms presumptive evidence of their pathogenicity." The aim of the work reported here was to collect further evidence on the significance of P.P.L.O. in pathological genital conditions and particularly in non-gonococcal urethritis (N.G.U.) in men.

It should be emphasized that N.G.U. is not a single syndrome. It is only negatively defined, for the term is applied to all cases of urethritis in which gonococci cannot be demonstrated. Harkness describes more than a dozen different kinds of urethritis in the male, including urethritis ab ingestis, traumatic urethritis, urethritis due to focal infection, protozoa, or bacteria, and infection due to a virus or to P.P.L.O., these last being probably transferred by sexual contact.

Material and Methods

Persons Investigated.—Specimens from patients at the London and St. Mary's hospitals were examined for the presence of genital P.P.L.O. by electron microscopy and by cultural methods. The electron micrographs often showed particles which might have been elements of a P.P.L.O. culture. However, P.P.L.O. elements are not defined by a special size, shape, or structure, and unless aggregated by natural growth or occurring in large numbers they cannot be reliably diagnosed morphologically. Furthermore, the cultural results could not be correlated with the electron microscopical picture. Therefore these studies were discontinued, and only the cultural method was used. Male patients suffering from N.G.U. and other congenital conditions, female patients from the venereal clinics with various complaints, and a group each of pregnant women and gynaecological patients were examined. A number of sexual consorts were included among the V.D. patients.

Methods of Culture.—The following medium was used: boiled blood, heart infusion, peptone agar (Klieneberger-Nobel, 1954), with the addition of 0.5% of "oxoid" yeast extract, using a filtered 10% stock solution (Edward, 1954); 20 μg. of desoxyribonucleic acid (D.N.A. per ml. (Edward and Fitzgerald, 1952); 20% inactivated pooled human serum (Klieneberger-Nobel, 1956); thallium acetate to a final concentration of 1 in 4,000 (Edward, 1954); 50 units of penicillin per ml. (Edward, 1954); 20% of a staphylococcus broth culture filtrate (Klieneberger-Nobel, 1956). This medium is very soft, a state well known to enhance the growth of P.P.L.O. Strains were also cultivated on the same medium without penicillin and thallium acetate, to determine their characteristic colony growth in the absence of these inhibitors. They were then established, by incubation while shaking, in a tryptic-digest horse-

*This work was carried out under the aegis of the Medical Research Council Working Party on Non-Specific Urethritis with the aid of a grant from the U.S. Public Health Service.

meat broth containing yeast extract, D.N.A., human serum, and penicillin in the concentrations given above. Human genital strains grow in this liquid medium with a characteristic slight turbidity within 24 hours. The broth cultures were stored at −20 to −30° C.: they remained viable for many months.

Procedure

In male patients discharge or scrapings were taken from the anterior urethra with a small platinum loop after cleaning the meatus with 70% alcohol. Specimens from the vagina, cervix, or urethra of female patients were also collected with a platinum loop. In cases of Reiter's disease synovial fluids and urethral discharges were examined. A number of blood samples from female patients in the venereal clinics were also cultured for P.P.L.O.

One of the difficulties of the examination of controls is the absence of any substantial amount of material that can be obtained for culture by scraping—a procedure that in any event may be impracticable, especially with the young male. The sensitivity of urine culture in revealing P.P.L.O. was established (*a*) by proving that human genital P.P.L.O. remained viable in urine, and (*b*) by parallel tests of discharge and urine in men attending a V.D. clinic.

To test the suitability of urine as a specimen for P.P.L.O. culture six human strains were suspended in filtered sterile urine. In six hours at room temperature (18–22° C.) the number of viable organisms fell to an average of 80% of the inoculum, which was approximately 100,000 organisms/ml. After 24 hours at this temperature approximately 50% of the organisms remained viable. In all of 14 strains viable organisms remained after 12 hours' incubation at 37° C. and in five of these more than 50% of the organisms were alive after this time. Accordingly, the sediments from patients' urines were invariably seeded on to nutrient medium within three hours of voiding.

The comparative examination of the yields of P.P.L.O. from urine and discharge was made in 66 male patients chosen at random.* P.P.L.O. were cultured from 18 of these. Both urine and discharge were positive in 11, only the urine in 4, and only the urethral discharge yielded P.P.L.O. in 3. Since approximately the same number of positive cultures were obtained from the urines as from the discharges we felt that urine was a satisfactory material for the detection of urogenital P.P.L.O. in the male, particularly as it had the advantage that specimens could easily be obtained, even from small boys.

About 30 ml. of each specimen of urine was centrifuged and the sediments were plated. The discharges and scrapings were inoculated on to fresh culture plates without delay. The synovial fluids were distributed on to solid and into liquid media. Subcultures to solid medium were made from the latter on three consecutive days. Specimens of blood were dispensed into liquid medium and similarly treated. The plates were incubated for seven days and were inspected by hand lens (×6) and microscopically (×56) by transmitted light.

Strains Isolated

Ninety-eight strains were isolated. All of those (40) so examined grew equally well aerobically and anaerobically. On the medium described they developed into microscopically visible colonies (about 200 μ in diameter) within 48 hours, provided the growth was not very dense. After three to five days the isolated colonies were about 500 μ in diameter. They grew larger with further incubation, and after seven days were readily visible to the naked eye and frequently were brownish yellow in colour. On the isolation medium the colonies have a slightly raised dark centre, under which the growth has penetrated into the agar, and a flat thin peripheral zone often marked with fine radiating lines. The edge is usually coarsely and irregularly broken, but sometimes entire. A few strains produce colonies with a fine structure consisting of translucent areas separated by darker lines giving the appearance of openwork lace, and resembling colonies of the L form of bacteria. All these colonies grow on the simpler stock medium with an entire edge.

In shaken broth culture at 37° C. the growth as a rule is slightly and uniformly turbid, but with a few strains it is finely granular. There is no growth at room temperature. Many strains grow on media enriched with horse serum, but some failed to grow unless human serum was used for enrichment.

There was no danger of confusing the P.P.L.O. with bacterial L-form colonies, with which they have certain properties in common (Klieneberger-Nobel, 1956), for in the few instances where P.P.L.O. colonies resembled L colonies they were distinguishable by their greater delicacy of structure. When coarser colonies, resembling those of the stable L forms of bacteria, were present, they all proved to be the so-called transformation forms induced by penicillin, and reverted to bacterial forms when cultivated on media not containing penicillin. No true L forms were seen in any of the primary cultures of the material.

The number of colonies from the discharges or urine sediments varied. Sometimes only a few were found. In most cases a considerable number, varying from many hundreds to many millions, developed. Bacterial colonies were found only rarely on the primary plates owing to the antibiotic and bacteriostatic contained in the medium.

A case was never diagnosed as P.P.L.O.-positive unless subculture on solid medium without penicillin and thallium acetate was established and the strain grew characteristically in liquid media as well.

Though workers sometimes feel able to distinguish between different species of P.P.L.O. by colony type and morphology, most of them conclude sooner or later that no dependable distinction can be made, because these characteristics vary with minute changes in the consistency and water content of the medium, and the density of growth. Strains may vary in colony type and exhibit differences of morphology in different sectors of the same plate. Some workers have used fermentation reactions, haemolysis, and growth inhibition by antisera for purposes of differentiation. In our hands none of these methods has proved to be reliable.

Two of the most constant characteristics we elicited from the strains were antibiotic sensitivity and antigenic structure.

Forty-eight of the strains were tested for antibiotic sensitivity by W. A. Blyth (to be published). All strains were resistant to penicillin, sulphonamides, erythromycin, and oleandomycin. The tetracycline group of antibiotics inhibited growth at concentrations of approximately 1 μg./ml. of medium, whereas

*These cases are not included in the tables.

streptomycin, chloramphenicol, spiramycin, and neomycin were less active, requiring 8–16 μg. for inhibition of growth.

Of our 98 strains, 56 were tested serologically by a complement-fixation method (D. H. Card, to be published); all of them cross-reacted to high titre with antisera to human genital P.P.L.O. and were serologically distinct from human mouth P.P.L.O. and also from animal and saprophytic strains. It was concluded that they formed a single serological group. It is noteworthy that all except one of Nicol and Edward's (1953) 91 human genital strains fell into one serological group. Huijsmans-Evers and Ruys (1956) found serological and cultural differences among the P.P.L.O. strains they isolated from the human genital tract, and they classified them into three groups, but the majority fell into one group.

Cultural Results in Men

Of 100 urines from apparently healthy adult males, three were positive for P.P.L.O. (Table I). One of them proved to have N.G.U. The second one was consistently positive in a series of tests; he had no symptoms during

TABLE I.—*Incidence of P.P.L.O. in the Urine of the Male (Control Groups)*

Age	No. Tested	P.P.L.O.-positive
Adults	100	3*
13 years or less	47	None

* One developed N.G.U.

this period, but had had attacks of prostatitis. No inquiry was made into the third case. Of 47 urines from boys under the age of 13 from the medical wards of the London and St. Mary's hospitals, none were positive. Clearly P.P.L.O. are rare in the genital tract of healthy men. Boys under the age of puberty who have had no sexual intercourse are free from P.P.L.O.

Of 201 discharges and scrapings from male patients from the venereal clinics, 52 (25.5%) were P.P.L.O.-positive (Table II). We divided the 201 cases on clinical grounds into the six groups shown in Table II. The highest number of positive results (48%) was obtained in the recently acquired N.G.U. group. In the

TABLE II.—*Incidence of P.P.L.O. in Urethral Discharges and Scrapings of Male Venereal Patients*

Group	No. of Cases	P.P.L.O.-positive	
		No.	%
Recently acquired N.G.U. ..	65	31	48
Untreated gonorrhoea	49	15	30·6
Miscellaneous conditions* ..	43	4	9·3
Reiter's disease	20	2	10
Chronic N.G.U.	17	0	
Cured ,, ...	7	0	
Total	201	52	25·5

* Epididymitis, chronic and low-grade prostatitis, penile sore and warts, and nine symptomless cases.

gonorrhoea group there were 30% positive P.P.L.O. cultures. The percentages in the groups of miscellaneous cases and Reiter's disease were much lower—namely, 9.3 and 10 respectively.

Six synovial fluids and all but two of 14 urethral discharges from cases of Reiter's disease were negative. The case histories of the two patients carrying P.P.L.O. are consistent with the assumption that the P.P.L.O. infection was superimposed on the Reiter's disease.

P.P.L.O. were not found in persons with chronic and cured N.G.U. However, the numbers tested are too small to be conclusive.

Cultural Results in Women

Two groups of women were examined—those attending the venereal disease clinics and those with other conditions such as pregnancy or gynaecological troubles. Of a total of 59 patients from the venereal clinics, 56% yielded a P.P.L.O. culture from the cervix, vagina, or urethra, or from a combination of these (Table III). In

TABLE III.—*Incidence of P.P.L.O. in Female Venereal Patients*

	No. of Cases	P.P.L.O.-positive	
		No.	%
Gonorrhoea, untreated	15	13	87
,, treated	9	8	89
Cervicitis and/or vaginitis and/or urethritis	11	9	82
Trichomonal vaginitis	6	2	33
Salpingitis	1	1	
Warts, ulcers	3	None	
No symptoms at examination ..	14	,,	
Total	59	33	56

untreated gonorrhoea (15 cases), in penicillin-treated gonorrhoea (9 cases), and in cases of cervicitis, vaginitis, or urethritis, or in a combination of these (11 cases), the proportions of P.P.L.O. cultures obtained were extremely high (87%, 89%, 82%). One case of salpingitis was positive. The six patients with trichomonal vaginitis were free from gonococci at the time of examination; two had P.P.L.O. in their discharge. Fourteen women who were completely free from symptoms and genital abnormalities (some of whom had been treated, possibly with a tetracycline) were P.P.L.O.-negative. Thus the incidence of P.P.L.O. in women suffering from venereal disease is generally very high. However, in an attempted

TABLE IV.—*Incidence of P.P.L.O. in Obstetric and Gynaecological Patients*

	No. of Cases	P.P.L.O.-positive	
		No.	%
Pregnant women	51	12	23·5
Gynaecological patients	58	10	17·3

isolation of P.P.L.O. from specimens of blood from 59 other female patients attending a V.D. clinic no positive cultures were obtained.

Of 51 pregnant women, 12 yielded cultures of P.P.L.O. from cervical specimens (23.5%), and 10 positive cultures were obtained from 58 gynaecological patients (Table IV). Thus approximately 20% of obstetric and gynaecological patients attending the London Hospital carry P.P.L.O. It was noted that several had trichomonal vaginitis or thrush.

Cultural Results in Consorts

Seven pairs of consorts were tested. In three pairs the male partner was suffering from recently acquired N.G.U., and P.P.L.O. were cultured from both partners. In the fourth pair of consorts the male partner had gonorrhoea, and P.P.L.O. were cultured from his discharge; his female partner also carried P.P.L.O. and developed abacterial cervicitis after penicillin treatment of gonorrhoea. In the three remaining pairs of consorts cultures for P.P.L.O. from both partners were negative. In one of the men a calculus was found which accounted for his purulent and haemorrhagic discharge. In the second pair the male partner had so little discharge that

treatment was thought to be unnecessary. In the third negative pair the male partner had chronic N.G.U. and low-grade prostatitis.

Discussion

Quite apart from N.G.U. there is evidence that P.P.L.O. can sometimes produce severe infections in humans. Stokes (1955) describes four cases in women. In one of them P.P.L.O. were isolated from the blood. Carlson, Spector, and Douglas (1951) reported two patients with Henoch–Schönlein purpura from whose blood P.P.L.O. were isolated on various occasions, and Gotthardson and Melén (1953) two patients with salpingo-oophoritis and with tubo-ovarian abscesses from which pure cultures of P.P.L.O. were cultivated. Dr. W. A. Gillespie, of Bristol Royal Infirmary (personal communication), isolated from a tubal abscess in a girl of 13 a pure culture of P.P.L.O. which in our hands proved to be of the same serological type as our genital strains.

We have shown that P.P.L.O. are found in almost 50% of men with recently acquired N.G.U. of short duration. In many of these positive cases the discharge contained pus cells but no visible organisms; in other cases bacteria were present, perhaps indicating a double infection. P.P.L.O. were also frequently present in men with gonorrhoea (30% positive); here the incidence was lower than in recently acquired N.G.U. Presumably, here also we are dealing with a double infection.

In striking contrast to this, almost all the healthy men of high hygienic standard and all the boys below the age of puberty were free from genital P.P.L.O.

We have confirmed the findings of Harkness and Henderson-Begg (1948), who found 50% positive in acute N.G.U. and no P.P.L.O. in 65 healthy controls (50 men and 15 women). Huijsmans-Evers and Ruys (1956) also report 50% of their N.G.U. cases positive. Nicol and Edward's (1953) interpretation of their own results is non-committal, but their incidence of positive cultures among various classes of people—though lower in N.G.U patients—is not strikingly different from ours. Their highest percentage of positive cultures, like ours, is in men with N.G.U. (26%). However, their group comprises all N.G.U. cases; the incidence of P.P.L.O. in recently acquired infections only may well have been higher. Nicol and Edward's lowest number of positives (11%) were found in a group of 90 police candidates without genital abnormalities, which they regarded as a control group of healthy men. It is, however, possible that if these men had been kept under observation before and after the examination some would have been found to have genital disease. This possibility is enhanced by the fact that two men gave a past history of N.G.U. and that a third was found at a later examination "to have developed signs of recurrence of this infection."

Freundt (1956) has published results which are in striking contrast to ours and to those of most other workers. He cultured P.P.L.O. more often from men with no genital abnormality than from those with N.G.U., acute gonorrhoea, or epididymitis. However, his results cannot be compared with ours, as he took his specimens from the external surface of the meatus and from the prepuce, whereas we cleaned the meatus and took samples with a platinum loop inserted 1 in. (2.5 cm.) into the anterior urethra. Moreover, he has not typed his strains.

A high percentage of P.P.L.O.-positive cases was reported by Shepard (1956, 1957). He described a new type of P.P.L.O. colony designated T type (T for tiny). We found no T-type colonies on our plates. His illustrations suggest that he has interpreted decaying cells from the discharge and scrapings as colonies, and has confused small bacteria and debris with P.P.L.O. elements in his stained preparations. He himself emphasizes that subculture was very difficult and was successful in only a few cases. In our experience, diagnosis of P.P.L.O. from pathological specimens was not possible by direct microscopical or electron microscopical examination.

The high percentage of positive cultures which we obtained in recently acquired N.G.U. in the male is very striking, particularly when the difficulties of diagnosis and the unreliability of the patients' statements are taken into account and when it is realized that proper controls are almost invariably negative. We conclude that the human genital P.P.L.O. are of significance in a considerable proportion of the cases diagnosed as N.G.U.

In agreement with most other authors we found that women carry P.P.L.O. much more frequently than men. This applies in particular to the women attending the V.D. clinics. In both untreated and penicillin-treated gonorrhoea the incidence of P.P.L.O.-positive cases was almost 90%. Like Nicol and Edward (1953) we also found P.P.L.O. in cases of trichomonal vaginitis. In cases of cervicitis, vaginitis, and urethritis the incidence was as high as 82%. Attention should also be drawn to the fact that P.P.L.O. could not be cultured in 14 women without symptoms at the time of examination and in two patients with genital ulcers and one with genital warts. This agrees with Harkness's results in 15 women without symptoms. P.P.L.O. were found in approximately 20% of gynaecological patients and pregnant women in the Whitechapel area. Compared with the percentage of positives in women with gonorrhoea, cured gonorrhoea, cervicitis, vaginitis, and urethritis this is a low figure.

Reiter's disease and N.G.U. are sometimes considered to have a common aetiology, and P.P.L.O. have been suspected as the most common cause of both conditions. Our cultural investigations offer no positive evidence for this hypothesis. P.P.L.O. were not found in any of the synovial fluids from patients with Reiter's disease which we examined, and only rarely from the urethral discharges in our cases of this condition.

Examination of blood from female patients in V.D. clinics has so far yielded negative results. Probably the occurrence of P.P.L.O. in the blood is rare, particularly in afebrile patients.

Conclusions

Genital strains of P.P.L.O. are (1) associated with recently acquired urethritis in a high proportion of men suffering from non-gonococcal urethritis; (2) associated with cervicitis, vaginitis, and urethritis in women; (3) likely to be transferred by sexual intercourse; (4) often associated with gonococcal infection and trichomonal infestation; and (5) absent in boys under the age of puberty and rare in healthy men and women.

I am indebted to my colleagues, Dr. G. Csonka, of St. Mary's Hospital, and Drs. J. K. Oates and R. D. Catterall.

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ACHALASIA OF CARDIA, CARCINOMA OF OESOPHAGUS, AND HYPERTROPHIC PULMONARY OSTEOARTHROPATHY

BY

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It is generally considered that carcinoma of the oesophagus is an unusual complication of achalasia of the cardia. A case of achalasia is described below in which carcinoma of the middle third of the oesophagus developed together with hypertrophic pulmonary osteoarthropathy.

Case Report

A man aged 26 first attended the out-patient department of Charing Cross Hospital in 1931 with a history of difficulty in swallowing for the previous six months. No abnormalities were found on physical examination. A diagnosis of achalasia of the cardia was made, and he was given a mercury bougie to use regularly.

During the next 23 years he remained well and did not attend the out-patient department again until November 16, 1954, when he stated that the bougie had broken about two months previously. Since then he had developed increasingly severe dysphagia, especially for solid food, and he had lost about 14 lb. (6.4 kg.) in weight. During this period he had also experienced pain and swelling in the ankles, knees, wrists, and finger-joints. He was adamant that daily use of the bougie in the past had ensured normal swallowing.

Examination showed a thin ill-looking man with marked clubbing of the fingers and toes as well as some swelling and tenderness and slight limitation of movements of the ankles, knees, wrists, and finger-joints. The chest showed generalized emphysema and bronchospasm. There were no palpable lymph nodes and examination of the other systems was essentially negative.

A fortnight later (December 2, 1954) he was admitted to hospital for further investigation. The following results were obtained: Hb, 12.4 g./100 ml.; red cells, 4,900,000/c.mm.; white cells, 16,900/c.mm. (polymorphs 68%); E.S.R., 27 mm. in one hour; serum uric acid, 3 mg./100 ml.; serum W.R., negative. A chest *x*-ray examination showed generalized emphysema with pleural thickening in the region of the oesophagus on the right side. The oesophagus was filled with food up to the level of the thoracic inlet and bulged to the right of the midline. A barium swallow showed that the oesophagus was dilated and tortuous, with evidence of oesophagitis. It was concluded that this appearance was due to achalasia of the cardia. Thin barium passed into the stomach without undue delay, but a mercury bougie could not be manœuvred below the lower third of the oesophagus even after the inhalation of octyl nitrite. There appeared to be a filling defect in the middle third of the oesophagus (Fig. 1). A series of *x*-ray films of the limbs showed evidence of new bone formation in the subperiosteal regions of the bones of the hands and feet as well as of the lower parts of the radius, ulna, tibia, and fibula. The changes were those of hypertrophic pulmonary osteoarthropathy (Fig. 2).

FIG. 1.—Barium swallow showing dilated oesophagus with appearance of filling defect in middle third of oesophagus.

During the next two weeks the patient received daily oesophageal lavages. At the end of this period screening examination of the chest showed that, although the oesophagus was still dilated and tortuous, a bougie could be passed through the cardia. The patient was using a bougie daily and finding that swallowing was becoming easier. On January 4, 1955, after a further fortnight of oesophageal lavages, oesophagoscopy revealed a large friable papilliferous growth involving the middle third of the oesophagus. A subsequent thoracotomy showed that the growth had spread into both hilar regions and was involving the pleura as well as becoming firmly attached to the aorta and vertebral bodies. No metastases were seen. The oesophagus was dilated and

FIG. 2.—Radiograph showing new bone formation at lower ends of radius and ulna.

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hypertrophied below the lower part of the growth and there was marked narrowing of the cardia, thus confirming the presence of achalasia. In view of these findings it was decided that resection of the growth was not possible, and surgical treatment was confined to a Heller operation. Histological examination of a biopsy of the oesophageal growth revealed a well-differentiated Grade I squamous-cell carcinoma.

After operation, swallowing continued to improve and a bougie was no longer necessary. However, the general condition of the patient remained rather unsatisfactory, and the clubbing as well as the pain and swelling in the distal joints persisted. A barium swallow three weeks after operation showed that gross oesophageal dilatation was still present, and, although there was no appreciable retention of barium, a very narrow area was still present immediately below the dilatation.

The patient was discharged from hospital on February 13. During the next two months he gradually lost strength, although he still swallowed without difficulty. He died at home on April 14. A post-mortem examination was not made.

Discussion

In 1872 Hilton Fagge described the development of carcinoma within a dilated oesophagus in a man of 84 who had experienced difficulty in swallowing for over 40 years. Since then several case records of a similar nature have been published (Rake, 1931; Baer and Sicher, 1947; Gore and Lam, 1952; Kastl, 1953; Klayman, 1955; Bohn, 1957). Although most of these authors concluded that carcinoma of the oesophagus was a definite complication of long-standing achalasia of the cardia, Groves (1956) felt that the risk of carcinoma developing in patients with achalasia could not be regarded as being greater than in the general population until further case reports were available. Indeed, Vinson (1942) believed that when carcinoma of the lower end of the oesophagus was found in patients with achalasia it could be assumed that the carcinoma was in fact the original lesion. However, this seems unlikely, since in most of the reported cases, including the one described here, there had been a long history of preceding difficulty in swallowing. Thus Baer and Sicher in a review of nine cases found that the shortest period from the onset of dysphagia until the discovery of malignancy was 10 years, while the average duration of symptoms was 19 years. Admittedly there was only a five-year history of dysphagia in one of the cases described by Klayman, but it is extremely unlikely that an oesophageal carcinoma existed throughout this period. As Baer and Sicher suggest, the apparent infrequency of an association between achalasia and carcinoma of the oesophagus may well be explained by the difficulties that beset the diagnosis of this combination.

Rake has emphasized the effects of stagnation of food and saliva in the oesophagus of patients with achalasia. He pointed out that the development of acute and chronic oesophagitis with ulceration is likely to be followed by attempted healing, which may in turn lead to papillomatous overgrowth of the epithelium. That author regarded the continual irritation of the oesophageal mucosa as a dangerous process which predisposed to carcinoma. In the majority of cases in which carcinoma has followed upon achalasia of long duration, the neoplasm has arisen in the middle third of the oesophagus. This site of predilection may be related to the fact that in patients with achalasia the column of food and fluid often extends as far up as the mid-oesophagus. It is conceivable that the fluid level causes a particularly marked degree of irritation of the mucosa. Although in the above case the patient had apparently remained free of dysphagia during the 23-year period of daily bougienage, it is quite possible that there was in fact a certain degree of intermittent retention of fluid in the lower half of the oesophagus. Thus it is well recognized that achalasia is sometimes asymptomatic, and occasionally a grossly dilated oesophagus is first discovered during the course of a mass radiography survey (Garland and Phillips, 1953). It is likely that the risk of carcinoma is negligible only in those patients in whom permanent dilatation of the cardia is achieved during the early stages of the disorder. Another factor which may have contributed to the development of chronic irritation of the oesophageal mucosa in this patient was the daily passage of a mercury bougie for a total period of 23 years. Indeed, such a possibility may constitute an additional reason for the early adoption of permanent dilatation in these patients.

If it is accepted that patients with achalasia occasionally develop carcinoma in the oesophagus, then it is important to appreciate the early manifestations of this complication. According to Baer and Sicher, suspicious symptoms include recurrence of dysphagia, more marked for solids than fluids, as well as blood-stained vomit, retrosternal pain, and excessive loss of weight. However, as Groves explained, the presence of the enlarged oesophagus may prevent aggravation of the dysphagia appearing as an early feature, swallowing not becoming really difficult until the cervical part of the oesophagus or the recurrent laryngeal nerves are involved. In the above case dysphagia developed after the breakage of the bougie but responded well to subsequent medical and surgical treatment, suggesting that this particular disability was due to the achalasia. Groves stated that an unexplained deterioration in the general condition of the patient may be the only indication that carcinoma has developed. Unfortunately, as Baer and Sicher stressed, even radiological examination of the oesophagus does not always exclude a carcinoma in the presence of well-established achalasia. In practice it is now generally accepted that oesophagoscopy is a more valuable diagnostic aid in these patients. Indeed, some authors, such as Rake, Gore and Lam, and Kastl, have suggested that oesophagoscopy should be carried out at regular intervals in all patients with achalasia, while Klayman has discussed the value of exfoliative cytological examination in the early diagnosis of oesophageal carcinoma. Klayman actually considered that this special technique should be employed annually as well as in the event of any exacerbation of symptoms in every patient with achalasia, in addition to radioscopy and oesophagoscopy. Certainly there seems no doubt that these patients should be seen at regular intervals, probably at least once every six months, and, if any suspicious features have developed, radioscopy and oesophagoscopy should be immediately undertaken. An important point emphasized by several authorities is the necessity for carrying out oesophageal lavage before either of these diagnostic procedures is performed, as otherwise a carcinoma may be missed.

It was probably a coincidence that the bougie of this patient broke less than four months before the diagnosis

of oesophageal carcinoma was established, although it is conceivable that the carcinoma offered additional obstruction to the passage of the instrument. Another possibility is that the carcinoma actually developed after the bougie had broken during the period when the achalasia was no longer under control. However, this sequence of events seems very unlikely, since examination of the chest contents at thoracotomy less than four months later revealed that the carcinoma had already extensively invaded the structures around the oesophagus.

It is generally accepted that hypertrophic pulmonary osteoarthropathy is rarely associated with diseases of the oesophagus. However, Brooks (1913) observed that hypertrophic osteoarthropathy was sometimes a feature in patients with mediastinal neoplasms which had invaded pulmonary tissue. Although in the above patient it is possible that clubbing had existed for a considerable period, the symptoms of hypertrophic osteoarthropathy were first noticed less than three months before his admission to hospital. For this reason it seems likely that the specific changes which developed in his distal bones and joints were associated with the spreading oesophageal carcinoma rather than with the achalasia. If this was so, the development of hypertrophic osteoarthropathy or even of simple clubbing should be regarded as highly significant in any patient with achalasia. Unfortunately, however, if the suggestion made in this case is correct, the appearance of these physical signs is likely to imply that the carcinoma has already spread to the pleura and pulmonary tissue. According to Flavell (1956) and Brea (1957), the severe joint pain of hypertrophic pulmonary osteoarthropathy may be relieved by vagotomy or hilar denervation. If this neurogenic theory is correct, it is not surprising that the pain in the limbs of this patient persisted after thoracotomy, since, although a Heller operation was performed, the hilar regions and the vagi were left intact.

Summary and Conclusions

A case of achalasia of the cardia of 23 years' duration is described in which carcinoma of the middle third of the oesophagus developed in association with hypertrophic pulmonary osteoarthropathy.

The occasional development of carcinoma of the oesophagus in patients with long-standing achalasia is emphasized. Although the early diagnosis of this complication is often difficult, regular observation of patients with achalasia is important. If a superimposed oesophageal carcinoma is suspected, oesophagoscopy as well as radioscopy, preceded by adequate lavage, should be promptly carried out. Exfoliative cytological examination may also be of value in these patients.

Probably the risk of carcinoma in patients with achalasia is negligible only in those in whom permanent dilatation of the cardia is achieved during the early stages of the disorder. It is possible that the daily passage of a bougie over many years further contributes to the development of chronic irritation of the oesophageal mucosa.

The development of hypertrophic pulmonary osteoarthropathy in patients with achalasia may be an indication that an oesophageal carcinoma has developed, with secondary spread to the pleura and pulmonary tissue.

I thank Dr. R. A. Hickling and Mr. Norman Tanner for permission to publish an account of this case.

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NOSE-BLEEDING AND HIGH BLOOD PRESSURE

BY

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Nose-bleeding is often said to be associated with high blood pressure. This belief is perpetuated by the standard textbooks of nasal disease and general medicine, in statements based on clinical impressions unsupported by objective quantitative data. One reads that epistaxis frequently accompanies high blood pressure (McLaggan and Collier, 1952); that hypertension is a common cause of nose-bleeding (Reading, 1953); that arterial hypertension often gives rise to epistaxis (Garland and Phillips, 1953); and that hypertension is the commonest systemic cause of epistaxis (Hunter, 1956).

This survey attempts to assess the validity of these statements by determining the frequency of nose bleeding in patients with high blood pressure, and the blood-pressure levels in patients presenting with nose bleeding.

Material

The hospital notes of two groups of patients were reviewed.

Series I: Patients Known to Have High Blood Pressure.—This group consisted of (*a*) 173 patients (86 males, 87 females) currently attending the hypertension clinic at Radcliffe Infirmary, and (*b*) 201 patients (89 males, 112 females) with diastolic pressures of more than 100 mm. Hg, culled from the patients admitted to the Radcliffe Infirmary in the 12-months period January–December, 1956. Of this subgroup, 143 (71%) were admitted because of high blood pressure, cardiac or cerebral vascular disease; 24 (12%) were admitted for surgical treatment; 20 (10%) for gynaecological procedures; 7 (3.5%) on account of diabetes mellitus, and 7 (3.5%) with skin conditions. The age structure of the whole series, comprising 374 patients (175 males, 199 females) is shown in Table I.

TABLE I.—*Age Incidence of 374 Patients with High Blood Pressure (Mean Age, 57.4 Years)*

Age (Years)	No. of Patients	Age (Years)	No. of Patients
Under 30	8 (2·1%)	60–69	99 (26·5%)
30–39	20 (5·4%)	70–79	47 (12·6%)
40–49	62 (16·5%)	80+	7 (1·9%)
50–59	131 (35·0%)		

Series II: Patients Presenting with Nose-bleeding.—In this group were 162 patients (86 males, 76 females) admitted to the E.N.T. department of the Radcliffe

Infirmary during the five-year period 1952–6 inclusive. The age structure of this group is shown in Table II.

TABLE II.—*Age Incidence of 162 Patients Presenting with Nose-bleeding (Mean Age, 53.4 Years)*

Age (Years)	No. of Patients	Age (Years)	No. of Patients
Under 10	7 (4·3%)	50–59	39 (24·0%)
10–19	4 (2·5%)	60–69	42 (25·9%)
20–29	5 (3·1%)	70–79	25 (15·4%)
30–39	13 (8·1%)	80+	9 (5·6%)
40–49	18 (11·1%)		

Methods

Series I.—From the documents, information was obtained about the occurrence of bleeding from the nose and from other sites, the blood pressure and the length of time for which it had been known to be high, and the level of the blood urea.

Series II.—From the documents the diastolic blood-pressure level just before the patient was discharged was obtained, thus excluding any errors due to the pressure being recorded during a period of acute blood loss. The pressure readings were then converted into an age- and sex-adjusted diastolic score (Hamilton *et al.*, 1954).

Note was also made of the local nasal state at the time of the bleeding—that is, whether there was a nasal abnormality such as a recent fracture, sinusitis, polyps, tumours, or deviated septum, or whether, apart from the bleeding-point, the nose appeared normal.

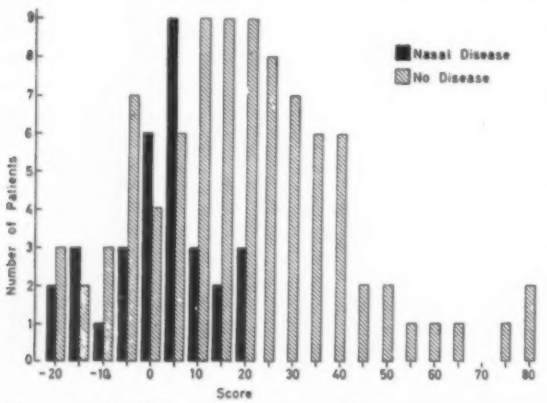
Results

Series I.—(1) *Nose bleeding:* Of this group of 374 patients with high blood pressure 17 (4.5%) had complained of nose-bleeding. For 8 of these it had been the presenting symptom which had led to the discovery of the high pressure. There was no correlation between the occurrence of nose-bleeding and the sex and age of the patient, the level of blood urea, or the length of time for which the high blood pressure had been known to be present. Of the 17 patients with nose-bleeding, 9 appear to have bled once only, the remainder having had recurrent bleeding. (2) *Bleeding from other sites:* 17 (4.5%) patients of the 374 had had gastro-intestinal bleeding, but in only three of these could any gut lesion be found. All the patients had had barium studies, and 3 of the 14 in whom these were normal had had exploratory operations, with negative results.

Series II.—41 (25.4%) patients out of this group of 162 patients presenting with nose-bleeding did not have their blood pressure recorded. Table III shows the level of diastolic pressure in the remaining 121, subdivided into those with nasal disease and those without. Because the age composition of the two groups is dissimilar, their blood pressure levels cannot be directly compared. It is, however, possible to correct for this age difference by translating each patient's diastolic pressure into an age-adjusted score, as described by Hamilton *et al.* (1954). The deviation, in mm. Hg, between an observed diastolic pressure and the mean for the general population at that age is adjusted to give a predicted deviation at the age of 60. This is the age- and sex-adjusted diastolic score, and the frequency distribution of these scores for patients with nasal disease and for those without is shown in the Chart. The mean age-adjusted score in the group with nasal disease was +2 mm. Hg, with a standard error of ±1.9; the mean score in the group with no nasal disease was +20 mm. Hg, the standard error being ±2.2. Standard error of the difference in means =2.9 mm. Hg, $p<0.01$.

TABLE III.—*Diastolic Blood-pressure Levels in mm. Hg of 162 Patients Presenting with Nose-bleeding*

Nasal Disease			No Nasal Disease		
Up to 95	Over 95	Not Recorded	Up to 95	Over 95	Not Recorded
30	2	8	25	64	33
Mean age of group 49·7 years			Mean age of group 57 years		



Frequency distribution of age- and sex-adjusted diastolic scores in 121 patients presenting with nose-bleeding.

Discussion

Series I.—Assessment of the frequency of a symptom by retrospective documentary studies cannot be expected to give a complete picture. It is probable that unless the nose-bleeding occurred just before the patient's visits to hospital, or was of considerable magnitude, it would not be complained of, and would therefore not appear in the records. It is of interest that in the documents of only two patients was the negative finding "no nose-bleeding" recorded, and the occurrence of nose-bleeding in approximately 5% of this group of patients with high blood pressure almost certainly underestimates its true frequency. In this series, in half of those in whom it occurred it was the symptom which made the patient seek medical advice and which led to the discovery of the high blood pressure. Gastro-intestinal haemorrhage, on the other hand, impresses itself more forcibly on both patient and attendant, and is therefore more likely to be recorded in the notes. The fact that it occurs with the same apparent frequency as epistaxis is, however, of interest, as is the high proportion of patients (14 out of 17) in whom no causal lesion could be found, despite full investigation. "Isolated haemorrhages" from the lung, renal tract, and gut, without apparent cause, have been said to occur in patients with high blood pressure (Hunter, 1956), but such bleeding, apart from that into the gut, was not found in this series.

Series II.—There is a clear-cut and striking difference between the distribution of age- and sex-adjusted scores in the group of patients with nasal disease and the group in which no local lesion was present. The patients with nasal disease are grouped about zero, indicating that their diastolic pressures are similar to those of a random sample of the general population. Those without nasal disease, on the other hand, clearly represent a different population, being grouped around a mean of +20 mm. Hg.

We may say, therefore, that in the absence of local disease nose-bleeding is associated with high blood pressure.

Summary

Seventeen patients (4.5%) from a group of 374 with high blood pressure had bled from the nose, and in 8 of these this was the presenting symptom. It is likely that these findings are an underestimate of the true frequency of epistaxis in these patients. Attention is drawn to the occurrence of gut-bleeding, in the absence of discoverable gastro-intestinal disease, in this group.

Thirty-two patients with nasal disease who were admitted to hospital because of nose-bleeding showed a normal distribution of age- and sex-adjusted diastolic scores. Eighty-nine patients without local nasal disease had an age- and sex-adjusted score distribution totally different from that of the general population.

Nose-bleeding, in the absence of local nasal disease, is therefore associated with high blood pressure.

I am grateful to Professor Sir George Pickering for advice and encouragement, and to Mr. R. G. Macbeth, Mr. G. H. Livingstone, and other members of the medical staff of the Radcliffe Infirmary for allowing me to study their case notes.

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THE DIAGNOSIS OF PSEUDOMYXOMA PERITONEI

BY

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Exactly a century ago Spencer Wells began his series of ovariotomies. Among the first 114 cases which he reported (Wells, 1865) there were two examples of pseudomyxoma peritonei. It was not, however, until 1901 that the same condition was found as a complication of an appendicular mucocele in a male patient (Fraenkel, 1901). Since that time reports of a single case or of a few non-gynaecological cases of pseudomyxoma have appeared at intervals, the largest series being that of Masson and Hamrick (1930), who described six cases from the Mayo Clinic. The exact nature of the material present in the peritoneal cavity is uncertain; it has variously been described as mucus, mucin, and pseudomucin. The origin of the mucinous material is also disputed, some pathologists believing that it is secreted by appendiceal cells which have been transplanted to the peritoneum, while other workers think that it is the product of a peritoneal reaction to irritation.

In many of the cases in which pseudomyxoma has developed in females with pseudomucinous cysts of the ovary, some appendicular lesion has also been present. A mucocele is found in about one out of every 1,000 appendices removed, and, as only a few mucoceles rupture, pseudomyxoma peritonei, which is not of ovarian origin, is a rare condition. A correct diagnosis is usually not made until laparotomy is performed. We recently observed two cases within a period of a few months; the experience gained with the first case enabled a correct pre-operative diagnosis to be made in the second.

Case 1

A 59-year-old man was admitted to hospital complaining of increasing abdominal distension and breathlessness, which had begun three months previously. He looked healthy, but his abdomen was strikingly enlarged, with an everted umbilicus and distended venous channels coursing upwards. A fluid thrill was easily elicited, but shifting dullness could not be demonstrated. No masses or abdominal organs could be palpated. A tense irreducible hernia was present on the right side, and there was oedema of both ankles.

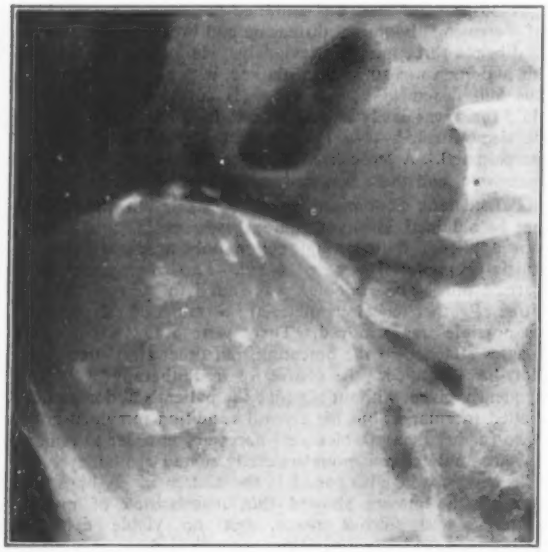
Paracentesis abdominis was performed, but fluid could not be obtained, even with the largest cannula, until suction was applied. With strong suction only a few millitres of mucinous material were obtained. Laparotomy was then carried out. The abdomen was found to contain about 4 litres of rather tenacious material; as much of this material as possible was removed. There were a few small cystic masses attached to the omentum, but other structures could not be identified. A course of radiotherapy was subsequently given, without benefit; the patient's abdomen continued to enlarge, but his general condition remained good. Two further laparotomies were necessary in order to remove the accumulated mucinous material; some large honeycomb-like masses were also found in the abdomen. A biopsy of one of the masses showed that it consisted of mucoid material and fibrous tissue, but no viable epithelial cells were seen. The operations were carried out at intervals of nine months, but at none of them was it possible to determine the origin of the condition. Symptomatically the patient was much improved after each operation, but six months after the last laparotomy his general condition had begun to deteriorate. Because of his large abdomen he was confined to a bath-chair at home.

Case 2

A 60-year-old man was admitted to a chest hospital on account of a productive cough and small haemoptysis. Full investigation did not reveal any pulmonary lesion, but a mass was noted in the right upper abdomen. He was therefore transferred to a general hospital. On admission there the patient looked fit and well. His abdomen, however, was grossly distended and the presence of an undefined mass in the upper abdomen was confirmed. A definite fluid thrill was present, but there was no shifting dullness. On rectal examination a firm mass could be felt projecting backwards from the recto-vesical pouch. Barium-meal radiographs revealed an indentation of the wall of the stomach; gall-stones were also present, and in the region of the lower pole of the caecum there was a calcified ring about 4 cm. in diameter (see Fig.). A diagnosis of pseudomyxoma peritonei was made and operation advised.

At laparotomy the abdomen was found to be filled with slightly greenish semi-translucent material of the consistency of a half-set jelly; several litres of this material were removed. There were numerous large plaques and masses like honeycombs adherent to and obscuring the omentum and intestines. It was impossible to locate any primary lesion, as the appendix and gall-bladder were hidden in masses of tissue. A biopsy from this tissue showed that it consisted mainly of mucinous material, with some fibrous tissue; in some places a well-differentiated intestinal type of epithelium was seen. Following this operation the patient

remained well for 11 months. He was then readmitted in a semiconscious and severely dehydrated state, the result of an acute obstructive episode similar to pyloric stenosis. His abdomen was still very distended, and several irregular masses were palpable. With gastric suction and correction of his fluid and electrolyte derangements his condition improved. A second laparotomy was carried out and 7 litres of mucinous material were removed. Analysis of this material showed it to contain 100 mg. of cholesterol and 12 mg. of calcium per 100 ml. After the second operation he felt much more comfortable but his general condition later began to deteriorate.



Radiograph showing incompletely calcified shadow in the right iliac fossa. Case 2.

Diagnosis

The case histories summarized above are, we believe, typical of pseudomyxoma peritonei. They reveal a reasonably consistent and characteristic clinical picture, but in spite of this, no report has been found of a correct diagnosis being made in a non-gynaecological case before paracentesis or laparotomy was performed. This failure to make a correct diagnosis is undoubtedly due to the rarity of the condition.

Pseudomyxoma peritonei usually occurs in patients over 50 years of age ; either sex may be affected. There is usually no definite history suggestive of abdominal disease ; only a few patients have had surgery carried out for ovarian or appendicular lesions. Painless abdominal distension is the commonest presenting symptom. The patient's abdomen has usually been enlarging for some months before he seeks medical advice. Edlund (1950) stated that colicky pain was often present. This type of pain is presumably due to bouts of subacute intestinal obstruction, which occur in the later stages of the disease.

Apart from his abdomen, the patient with pseudomyxoma peritonei looks healthy. He is well nourished and there is no evidence of cyanosis or anaemia. In marked contrast to the general appearance of well-being, the abdomen presents a typical picture of advanced disease. It is grossly distended with fluid, and irregular masses can often be palpated on abdominal and rectal examination. In the age group affected abdominal distension may be due to cancer with ascites, cirrhosis of the liver, or heart failure, but in none of these conditions does the patient maintain a generally healthy appearance for many months or years. It is the remarkable disparity between the healthy look in the patient's face and the seemingly hopeless findings in his abdomen which should suggest the correct diagnosis of pseudomyxoma peritonei.

Valuable confirmatory evidence may be obtained by testing for fluid in the abdomen. In almost all cases a well-marked fluid thrill is easily elicited, but when the test for shifting dullness is carried out the dullness will not shift (Elliott, 1957). It should be remembered, however, that these tests for fluid will vary with the viscosity and total amount of mucus within the abdomen, and on the extent to which the mucus has become organized. Mucus of low viscosity might give a positive test for shifting dullness ; when its consistency is that of a half-set jelly it no longer moves about within the abdomen, but still transmits a fluid thrill. Work is now in progress to determine whether the intraperitoneal production of mucus can be inhibited by serotonin antagonists and whether the mucus can be rendered more fluid by the administration of hormones and enzymes.

The raised intra-abdominal pressure elevates the diaphragm and interferes with respiratory movement ; breathlessness may result as in Case 1. An external hernia may develop for the same reason, and several cases have been diagnosed by the surgeon finding mucinous material within a hernial sac. Mucinous material can enter and track down inside the psoas sheath, and present as a lump in the thigh (Masson and Hamrick, 1930 ; Palmer *et al.*, 1958). Major veins are sometimes compressed ; oedema of the legs is not uncommon, and in Case 1 abnormal venous channels had opened up in the abdominal wall. Three out of the four patients with pseudomyxoma peritonei described by Edlund (1950) had frequency of micturition which was probably due to bladder compression. In the later stages of the disease the adherent masses of tissue often distort and obstruct various parts of the alimentary canal, and intestinal obstruction is the commonest cause of death.

Biochemical investigations are seldom helpful. Rosenfeld (1949) has stated that the blood sugar may be abnormally low and there may be alterations in the albumin : globulin ratio. Straight *x*-ray examination of the abdomen of the patient reported by Tedeschi *et al.*, (1949) showed an incomplete circular shadow in the right iliac fossa similar to that noted in our second case. This type of shadow is probably due to calcification in the wall of an old appendix abscess or mucocele (Ogilvie, 1915) or in the fibrous tissue surrounding and encysting some of the mucinous material. Faulkner *et al.* (1954) noted a similar type of shadow in their patient who had a urachal cyst causing pseudomyxoma peritonei. Once the mucinous material has become organized into honeycomb-like masses, barium-meal or barium-enema examination may reveal indentations and distortions of the alimentary tract. Gallstones and duodenal ulcers have been found in several patients.

A correct diagnosis of pseudomyxoma peritonei during life has usually been made only when the abdomen has been explored by paracentesis or laparotomy. In some of the reported cases the mucinous material has been of sufficiently low viscosity to flow

through a cannula. However, in other patients, such as those reported above, the viscosity of the intraperitoneal material is such that ordinary paracentesis fails to produce any fluid. When a "dry tap" is obtained on an abdomen showing a fluid thrill, the possibility of pseudomyxoma should at once be considered, and gentle suction applied to the cannula in an attempt to draw off some of the mucinous material. The diagnosis may be confirmed by peritoneoscopy (Tedeschi *et al.*, 1949).

At laparotomy the diagnosis is of course obvious, but the surgeon may be in some doubt whether he is dealing with a benign or a malignant condition. It now seems probable that most cases of pseudomyxoma peritonei are benign. A mucocele of the appendix should always be sought, and in females the pelvis should be examined for a pseudomucinous cyst. It was formerly believed that many cases of pseudomyxoma peritonei were due to ruptured colloid carcinomas of the appendix (Masson and Hamrick, 1930; Woodruff and McDonald, 1940), but, as with minimal surgery these patients lived for many years, it seems likely that the tumours were either carcinoid or organized mucinous masses containing hyperplastic but benign epithelial elements. When the mucinous material is very tenacious or has become partly organized proper exploration of the abdomen may be impossible.

Summary

The diagnosis of pseudomyxoma peritonei is described and two typical cases are reported.

There is a striking contrast between the general well-being of the patient and the advanced signs present in the abdomen.

When a fluid thrill is present in the abdomen failure to demonstrate shifting dullness or to withdraw fluid on paracentesis should suggest the diagnosis.

We thank Dr. J. S. Logan, Royal Victoria Hospital, Belfast, for permission to report Case 1, and Mr. T. L. Kennedy and Mr. J. M. Megaw for performing several of the laparotomies.

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In future the British Commonwealth and Empire Nurses War Memorial Fund will be known as the British Commonwealth Nurses War Memorial Fund. The Fund was founded in 1946 to provide a worthy memorial to the nurses, midwives, and auxiliaries of the British Commonwealth who died in the second world war. The memorial consists of a Nurses' Chapel in Westminster Abbey, and a trust fund which awards postgraduate travelling scholarships to nurses and midwives of the Commonwealth. Up to date 84 scholarships have been awarded, and 11 more are announced for the academic year 1959–60.

TWINNING RATE IN EUROPE DURING THE WAR

BY

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It is known that undernutrition causes a decrease in the litter size in many mammals (Hammond, 1952; Lack, 1954). The purpose of this paper is to determine whether there was a decrease in the twinning rate in man in those countries which suffered from undernutrition during the German occupation during the last war.

Data on twinning rates are reported here for Denmark, France, Holland, Norway, and Sweden. There was little or no undernutrition in Denmark, which was leniently treated by the Germans (Fridericia, 1947), or in Sweden, which remained neutral (Abramson, 1947). There was, on the other hand, considerable undernutrition in France (Trémolières, 1947), Holland (Jansen, 1947), and Norway (Hansen, 1947). There is also considerable evidence of regional variation in the amount of malnutrition in France: in particular, the north-west (Brittany and Normandy) is believed to have suffered little (Chevallier and Moine, 1945; Trémolières, 1947); data for this region of France are given separately.

Methods.—Data on twin maternities by sex, and on total maternities by maternal age, were taken from the annual reports on vital statistics of the countries concerned. Monozygotic and dizygotic twin maternities have been calculated by Weinberg's method (1909), which assumes that dizygotic twins are equally likely to be of the same or of different sexes; monozygotic twins must of course be of the same sex. If, therefore, L like-sexed and U unlike-sexed twin maternities are observed, the number of dizygotic twin maternities is taken as $2U$ and the number of monozygotic twin maternities as $L-U$. The sex of twins is not available for Denmark, and so this method cannot be applied. All rates are expressed as twin maternities per 1,000 maternities, and have been standardized for maternal age by the indirect method of standardization (see Hill, 1955). The standard twinning rates used are those for France by maternal age reported by Bulmer (1958).

Results

The monozygotic and dizygotic twinning rates for the five-year periods before, during, and after the war are shown in Fig. 1. The wartime quinquennium is taken as 1941–5. The post-war quinquennium is 1946–50. The pre-war quinquennium is 1936–40 in all countries except France, where it is 1934–40, excluding 1937 and 1938, for which years data are not available.

The total twinning rate is smaller during the war than either before or afterwards in France, Holland, and Norway. The fall is largest in Norway and smallest in France, but in all three countries it is significant at the 0.1% level. In Denmark, Sweden, and North-West France the twinning rate seems to be falling over the period considered, but this decrease is not accentuated during the war.

It can also be seen that the fall in France, Holland, and Norway is entirely due to a fall in the dizygotic

twinning rate; indeed, the monozygotic twinning rate rises, if anything, in France and Holland, although this is not statistically significant. Thus the dizygotic, but not the monozygotic, twinning rate fell during the war in three countries which were undernourished, but not in Denmark or Sweden, nor in the North-West of France, which were comparatively well nourished.

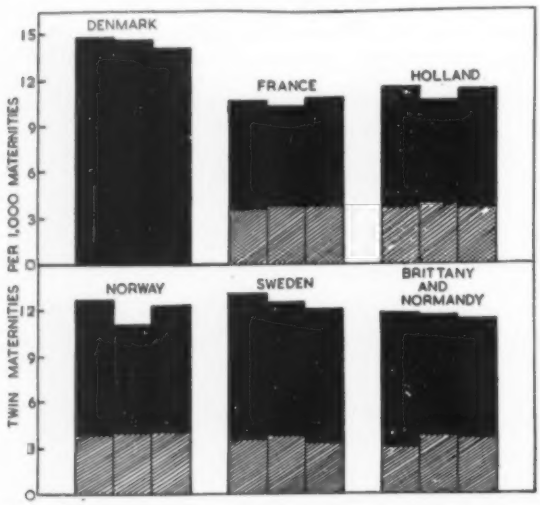

FIG. 1.—Monozygotic (hatched) and dizygotic (black) twinning rates. Only the total twinning rate is available for Denmark.

The yearly twinning rates for France, Holland, and Norway are given in Fig. 2. In general it can be seen that the dizygotic twinning rate falls sharply in 1941; there is a slight further fall in 1942, and the rate then remains constant until 1946, when it rises again, and returns to its pre-war level in 1947. The depression in Norway in 1942 is probably not real, since it is not reflected in the total twinning rate. (It must be remembered that the estimates of the monozygotic and dizygotic rates are negatively correlated, and that a simultaneous rise in one accompanied by a fall in the other may therefore well be a sampling error.) It is, however, tempting to attribute the depression in Holland in 1945 to the "famine winter" of 1944–5, when there was severe starvation in Western Holland (Banning, 1947).

Discussion

It has been shown that there is a fall in the dizygotic twinning rate in three countries (France, Holland, and Norway) which suffered malnutrition during the war, but not in Denmark or Sweden, nor in the North-West of France, which were comparatively well-nourished. It is difficult to resist the conclusion that the fall in the twinning rate was directly caused by the malnutrition. It is suggested that this decrease is due to a decreased tendency of the ovary to produce double ovulations, due perhaps to a diminished secretion of gonadotrophin by the pituitary, which is known to follow prolonged underfeeding in animals (Burrows, 1945). There are, however, two other explanations which cannot be ruled out: (1) a decrease in male fertility; and (2) an increased prenatal mortality. In the latter case the increased mortality must be restricted to a very early period, before the embryo divides to give monozygotic twins, since there is no decrease in the monozygotic twinning rate.

Summary

The dizygotic twinning rate fell during the war in France, Holland, and Norway, but not in Denmark, Sweden, or the North-West of France; the monozygotic twinning rate remained constant in all these countries. It is suggested that this was due to a decreased tendency of the ovary to produce double ovulations, which was caused by undernutrition.

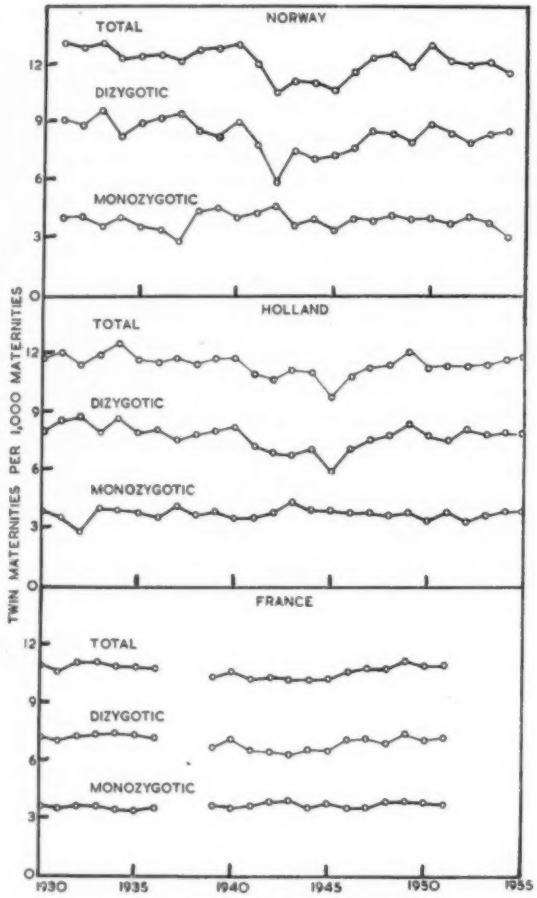

FIG. 2.—Yearly twinning rates.

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STABILITY OF THE POTENCY OF POLIOMYELITIS VACCINE

BY

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In most countries poliomyelitis vaccine is given an expiry date of six months from release, provided that the storage temperature approximates to 4° C. So far this has caused little inconvenience, since the demand has exceeded the supply. When, however, the supply exceeds the demand a more realistic expiry date would be desirable. Some knowledge of the precautions that must be taken with the transportation of vaccine, especially to tropical countries, is also required. A study was therefore made of the loss in antigenic potency of vaccine stored at different temperatures.

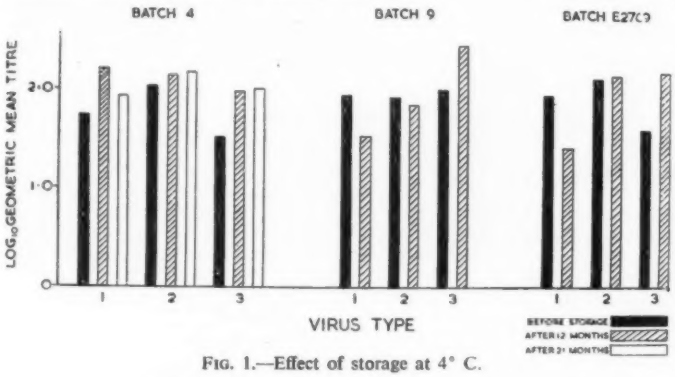

FIG. 1.—Effect of storage at 4° C.

Materials and Methods

Storage of Vaccine.—Three different batches of formalin-inactivated vaccine were tested: batches 4 and 9, prepared in Britain by the Glaxo Laboratories, and batch E2769, in the United States of America by Eli Lilly and Company. All three batches contained MEF-1 and Saukett as the type 2 and 3 components respectively; as the type 1 component the British batches contained the Brunenders, and the United States batch the Mahoney strain. All were preserved with thiomersolate and "versene." At the beginning of the storage period each batch was tested for antigenic activity. Samples from all three batches were stored at 4° C. and tested after 12 months, and an additional test was made with one of the batches after 21 months. Samples from batch 9 were also stored at room temperature (approximately 21° C.) and 31° C.; after 40 and 100 days at each temperature they were refrigerated at 4° C. and held at this temperature for three to five months, when the activities of all samples were tested in parallel.

Tests for Antigenic Activity.—For each test, groups of rhesus monkeys were injected with vaccine by the method in current use in the United States of America (U.S. Public Health Service, 1956). Each group consisted of 9 to 12 monkeys taken from the same consignment, weighing between 4 and 8 lb. (1.8 and 3.6 kg.). Before their course of injections the animals were shown to have no detectable poliomyelitis antibodies. They were given three intramuscular injections of vaccine, each of 1 ml., at intervals of seven days, and sera were collected seven days after the last dose. Sera were titrated for poliomyelitis neutralizing antibodies to each virus type by the method routinely used in this laboratory (Biological Standards Control Laboratory, 1957; Perkins, Sousa, and Tobin, 1958). In order to obtain comparable results, the sera from all monkeys were titrated against each virus type in one test, using a reference serum as a control. Mixtures of serum dilutions and virus suspensions were held at 37° C. for three hours and overnight at 4° C. before being added to the monkey-kidney-cell cultures, which were then incubated at 37° C. in roller drums and examined after seven days. Titres (PD_{50}) of sera are expressed as the dilution of serum in the serum–virus mixtures before addition to cell cultures and the activity of each sample of vaccine as the geometric mean titre produced by the group of monkeys.

Results

Fig. 1 gives the results of tests made with samples from all three batches before and after storage at 4° C. Taking into account the variation which is often encountered in the response of monkeys to poliomyelitis vaccine, there was no evidence, with any of the three batches, of a loss in antigenic activity during 12 months at this temperature; neither was there evidence of a loss with batch 4, which was stored for 21 months.

At higher temperatures of storage, however, a decline in potency was observed (Fig. 2). Although storage at 21° C. had no detectable effect on the activity of the type 2 and 3 components even after 100 days, this temperature considerably reduced the activity of the type 1 component after 40 days' storage and brought about a still further reduction after 100 days. At 31° C. the decline in activity was more striking. After storage for 40 days there was a considerable decline in the type 1 activity, less with the type 2, and none detectable with the type 3; after 100 days, however, the activity of all three types was completely lost.

Conclusions

The results of these tests indicate that poliomyelitis vaccine may be stored at 4° C. for at least 12 months

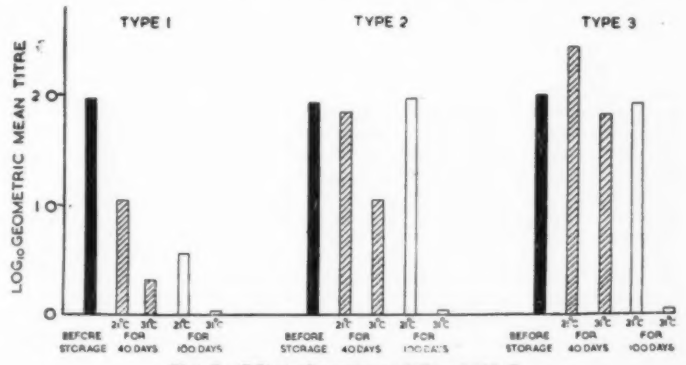

FIG. 2.—Effect of storage at 21° and 31° C.

without a detectable loss occurring in the antigenic activity of all of its three components. It is suggested that refrigeration at 0° C. to 10° C. would be equally suitable. At higher temperatures, such as 21° C. and 31° C., the activity is much less stable, especially in the case of the type 1 component.

It is important, therefore, that transportation of unrefrigerated vaccine in temperate climates should be carried out in as short a time as possible. Since considerable reduction in the activity of the type 1 component was found to occur after 40 days' storage at 21° C., it is suggested that vaccine should not be held unrefrigerated for periods longer than seven days.

It is also suggested, in view of the rapid loss in activity which was shown to occur at 31° C., that transportation of vaccine in tropical climates should not be carried out without refrigeration facilities.

We thank the Glaxo Laboratories and Eli Lilly and Company for the supply of poliomyelitis vaccine. We also thank Miss K. South and Miss P. Tumber for their technical assistance.

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Medical Memorandum

An Unusual Cause of Solitary Hepatic Abscess

Hepatic suppuration is an uncommon condition, and solitary hepatic abscess comprises a small proportion of this group. The following case of solitary hepatic abscess was of such unusual aetiology that it is recorded.

CASE REPORT

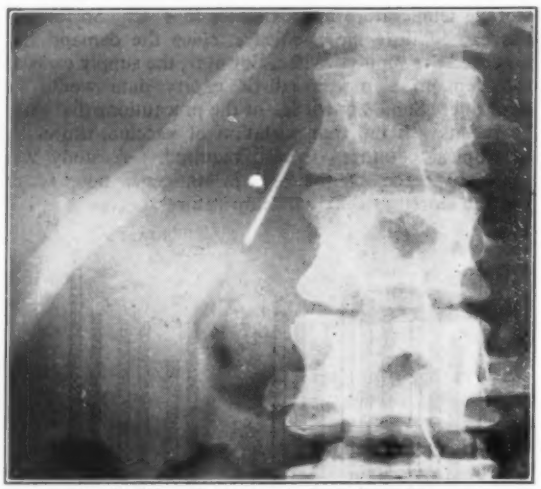
A man aged 34 was admitted from the casualty department on June 27, 1957, with a history of recurring attacks of epigastric pain in the previous six weeks. An attack had occurred on most days, lasting a variable number of hours; the pain was severe, sustained in its intensity, and radiated into the upper lumbar region. It had no relation to meals, activity, or personal habits, and it was not relieved by antacids or food. There had been no nausea or vomiting. His bowel habit was regular, and he had had no disturbance of micturition. A particularly severe attack of pain lasting six hours caused his admission to hospital.

On admission the patient was not in obvious pain; mouth temperature was 100.4° F. (38° C.). No abnormality was seen on inspection of the abdomen. Palpation revealed tenderness with guarding of the epigastrium and beneath the right costal margin. There were no physical signs elsewhere in the abdomen. The rest of the physical examination revealed no abnormalities; urinalysis was negative; Hb, 12.4 g./100 ml.; W.B.C. 15,000/c.mm. (neutrophils 70% and monocytes 10%).

A provisional diagnosis of "leaking" peptic ulcer was considered and a radiograph of the abdomen carried out to detect free air under the diaphragm. A gas shadow was not seen, but the antero-posterior film did reveal a sewing-needle lying to the right of the first and second lumbar vertebrae. The air-filled duodenal cap was seen below the needle, suggesting that the needle was outside the gastro-intestinal tract (see Fig.). On further questioning, the patient admitted that he had for several years swallowed objects, mainly needles, as a trick in public-houses; he stoutly denied that any harm had resulted from this pastime.

On the assumption that he had a perigastric abscess a laparotomy was performed (Mr. K. F. Wood). In fact, a large tense fluctuant swelling (15 cm. in diameter) was found within the lobes of the liver. There were a few flimsy adhesions between the first part of the duodenum and the underside of the liver but without evidence of a perforation of the stomach or gut. Pus was obtained on aspiration of the swelling. The abscess was then excluded from the peritoneal cavity by packs and drained externally by a rubber tube. A needle 4.5 cm. long was found embedded in the wall of the abscess. Post-operatively the liver-function tests were normal and culture of the pus showed it to be sterile. The patient made an uneventful recovery and left the hospital on July 27.

Biopsy of abscess wall (Dr. O. G. Dodge) was reported to have the appearances of a non-specific subacute liver abscess.



Needle lying above gas shadow of duodenum.

COMMENT

Pyogenic abscesses of the liver are relatively uncommon. Ochsner, DeBakey, and Murray (1938) found 42 cases in half a million admissions during a 10-year period at the Charity Hospital in New Orleans. In these and other statistics (Rothenberg and Linder, 1934; Eliason *et al.*, 1938; Kisner, 1947; Yarvis, 1953) both multiple and solitary abscesses are grouped together, although it is clear that multiple lesions arising usually from appendiceal or gall-bladder infections greatly outnumber solitary ones.

Penetrating injuries from without occasionally result in a solitary hepatic abscess; there is, however, only one previous record (Morris, 1940) of the transperitoneal migration of a foreign body—in this case a toothpick—from the gastro-intestinal tract to the liver. As in the above case, there was no naked-eye evidence of perforation on the gut surface, although there was marked adherence of the colon, omentum, jejunum, and pancreas to the abscess site.

I thank Professor R. P. Jepson and Mr. K. F. Wood for their encouragement and help in writing this report.

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Reviews

PAINLESS LABOUR

Psychoprophylactic Preparation for Painless Childbirth: Its Theory and Practical Approach with the Complete Course of Lectures. By Isidore Bonstein, M.D. (Pp. 143; illustrated. 12s. 6d.) London: William Heinemann Medical Books, Ltd. 1958.

Painless Childbirth. By Fernand Lamaze, translated by L. R. Celestin, M.B., B.S.Lond., F.R.C.S.Edin. (Pp. 190; illustrated. 12s. 6d.) London: Burke. 1958.

Les Méthods Psychosomatiques d'Accouchement sans Douleur: Histoire, Théorie et Pratique. By L. Chertok. Second edition, revised and enlarged. (Pp. 348+xvi; 2,200 fr.) Paris: L'Expansion Scientifique Française. 1958.

Our colleagues on the Continent have taken up with enthusiasm the question of preparing mothers for "painless labour." The method known as "psychoprophylactic preparation" derives from Russia, is based on Pavlovian physiology, and attempts, by intensive education, to replace the conditioned reflex in which uterine action is felt as pain by another in which uterine action is felt as a painless sensation. This teaching is strongly reinforced during labour. The mother is also taught a special kind of breathing to use during contractions which she is persuaded will help her and which firmly holds her attention. There is, of course, a great deal more to it than this in its application and psychological management. The late Dr. Lamaze introduced the method, with modifications, into his Paris clinic, and from there it spread widely. Controversy wages fiercely over the relative merits of this method and the "Dick Read method."

Dr. Bonstein's little book gives a short but fairly accurate account of the teaching at Dr. Lamaze's clinic and describes its trial at Cleveland, Ohio. A fuller and more authentic account, written by Dr. Lamaze's team before it disbanded, has been translated into English and published under the title "Painless Childbirth." It confirms the impression that is sometimes received by onlookers of the method that it can lend itself to a sort of "brain-washing." It is apparently necessary for its success to refute all other methods, and the chapter which purports to analyse a British one describes chiefly its abuses and misapplications. Nevertheless, the author's own scheme is, in practice, often highly successful. Because it came to countries that previously had not, perhaps, paid so very much attention to relief of pain in labour, the method had a greater impact and was therefore applied with a refreshing enthusiasm. The need to avoid the obvious dangers of exaggeration and over-enthusiasm provides a splendid reason for doing nothing. In this country, where we have had for some while methods capable of as good results or better, advances—in practical use of analgesic agents as in theories of management of labour—that once met with opposition are now given lip-service, and that is often regarded as sufficient. The term "painless labour" is a stumbling-block to many—and also provides a fine refuge from the effort of examining the matter further.

Dr. Chertok is a psychiatrist who has especially interested himself in psychosomatic medicine, and lately in its particular application to maternity. In his book describing the psychosomatic methods of achieving painless labour he has surveyed the whole field very extensively. Though this means that at times he has to skim his sources only lightly his achievement is remarkable and stimulating. He makes many brilliant analyses and seeks to show that the underlying principles in all the methods are very similar. Studies such as this suggest possibilities of further investigation and understanding of a subject that to women remains one of inescapable interest. An English translation of Dr. Chertok's book is appearing shortly.

SHÎLA RANSOM.

PRACTICAL OBSTETRICS

Obstetric Practice. By H. Bruce Williams, M.B., Ch.M., F.R.A.C.S., F.R.C.O.G. Foreword by Professor F. J. Browne. (Pp. 168+viii; illustrated. 21s.) Sydney, London, Melbourne, Wellington: Angus and Robertson. 1957.

This small book is concerned entirely with the practical side of obstetrics and is designed for general practitioners working in the conditions obtaining in Australia rather than in Great Britain. It represents the fruits of the experience of an obstetrician of the older school. These are sometimes expressed dogmatically in note form, sometimes written in such a chatty informal way as to make the reader think he can hear the author speaking. Unfortunately, Dr. Bruce Williams will speak no more. This book reaches us after his death, and it makes a fitting memorial to one who in life had a warm personality, who was kindly, direct, honest, and courageous. All these characters are mirrored here, and if the classification of diseases and the treatment advised are not always in keeping with modern thought and knowledge, does it really matter? In compensation there are the jottings from the notebook of a good doctor, and many gems of wisdom born of a sympathetic and understanding care of innumerable women during pregnancy and labour.

T. N. A. JEFFCOATE.

WORK ABILITY OF THE AGED

Ageing and Human Skill. A Report Centred on Work by the Nuffield Unit for Research into Problems of Ageing. By A. T. Welford. (Pp. 300+vi; illustrated. 25s.) London: Oxford University Press. 1958.

Ageing and Human Skill, published by the trustees of the Nuffield Foundation, is a record of researches into the many questions on the result of ageing on human skill and performance as related to work. Many studies have been made earlier, but this report gives the present position of knowledge in this fascinating field, and, as Welford says in his concluding remarks, "we must observe as accurately and objectively as we can, searching forward step by step, content never to be quite sure where we shall eventually arrive." The subject-matter of this report is of profound importance in view of the changing age structure of the population and its impact upon the economy of the nation. The work describes methods and results obtained in a series of research studies, and includes such subjects as age changes in performance, the nature of skill, speed and accuracy of movement, some implications of slowing, perception, problem solving, learning and memory, and adaptability. The explanatory figures and tables are very good and greatly add to the reader's appreciation of the work done. The many references to other studies and research enlarge the horizon and add to the general interest of the subject.

The high standard of the work undertaken and the excellent presentation make the book one which will appeal to and interest many different types of workers in the field of gerontology, including medical personnel

and those who are concerned in industry. In spite of the scientific nature of the research and the manner of presenting factual data, there is also running through the work a humanistic approach which makes it an outstanding contribution to the subject and a book which should be studied very widely and kept for reference.

MARJORY W. WARREN.

E.E.G. STUDY OF TWINS

Über die Erblichkeit des Normalen Elektroenzephalogramms. Vergleichende Untersuchungen an Ein- und Zweieiligen Zwillingen. By F. Vogel (Pp. 92; illustrated. DM. 9.60.) Stuttgart: Georg Thieme Verlag. 1958.

This is a careful study of the electroencephalograms of more than 200 pairs of identical and non-identical twins. As would be expected of its famous place of origin, the method of working is impeccable both as regards the study of zygosity and electroencephalographic technique. Unfortunately the aims of the investigation were apparently limited to what is already generally accepted —namely, that there is a large genetic contribution to the appearance of the normal electroencephalogram. The work does not add to our knowledge of any possible genetic mechanisms or of any neurophysiological correlations. Almost the only new addition to knowledge seems to be the disproof of the fact that the increased amplitude of alpha rhythm often found on the right side compared with the left is not significantly related to handedness, nor were any mirror image electroencephalograms found in identical twins.

D. A. POND.

CLINICAL CHEMICAL METHODS

Clinical Biochemical Methods. By A. L. Tárnoky, B.Sc.Tech., Ph.D. (Pp. 239; illustrated. 50s.) London: Hilger and Watts Ltd. 1958.

There are many books describing laboratory techniques, and the publication of yet another one would seem to require some justification. It must be said at once that this book justifies itself immediately by its simplicity of presentation and the terse directness of its style. Dr. Tárnoky is the biochemist at the Royal Berkshire Hospital, and his book is a compilation of the clinical chemical methods in routine use in his department. Each method is described in the form of notes beginning with a brief account of the underlying principle and the type of specimen required. Instructions for the techniques are written in the imperative mood, and are followed by the method of calculating and expressing the results with the normal findings. The reagents are listed, and finally there are helpful comments on special aspects of each technique. Each method is ascribed to its author, and there is a bibliography of 84 references at the end of the book, five of them being to original work by Dr. Tárnoky himself. There is a short section on analytical control, and a list of manufacturers of equipment and chemicals, and of books in everyday use in the author's laboratory. There is, deliberately, no clinical interpretation of the results. In spite of its surely unnecessarily high price, this is a very useful manual of English routine practice in a clinical chemical laboratory, and it should have a wide appeal to clinical pathologists throughout the country. Medical laboratory technicians working for their diplomas in chemical pathology will find it invaluable.

WALTER H. H. MERIVALE.

BOOKS RECEIVED

Review is not precluded by notice here of books recently received

Physical Diagnosis. By F. D. Adams, M.D. 14th ed. (Pp. 926+xiii; illustrated. 96s.) London: Baillière, Tindall and Cox.

Lung Function Tests. An Introduction. By B. H. Bass, M.D., M.R.C.P. (Pp. 72+viii; illustrated. 8s. 6d.) London: H. K. Lewis and Co. Ltd. 1959.

Trifluoperazine. Clinical and Pharmacological Aspects. Twenty-five original reports, with an introduction by Henry Brill, M.D. (Pp. 215. 26s.) London: Henry Kimpton. 1958.

Convulsive Disorders of Children. By Dora Hsi-Chih Chao, M.D., R. Druckman, M.D., and P. Kellaway, A.M., Ph.D. (Pp. 151+vi; illustrated. 42s.) Philadelphia, London: W. B. Saunders Company. 1958.

Handbook of Obstetrics and Gynaecology for Nurses. By D. G. W. Clyne, B.M., B.Ch., M.A., L.R.C.P., F.R.C.S., M.R.C.O.G. (Pp. 204+v; illustrated. 15s.) Bristol: John Wright and Sons Ltd. 1958.

Leukemia. By W. Dameshek, M.D., and F. Gunz, M.D., Ph.D. (Pp. 420+xi; illustrated. $15.75.) New York, London: Grune and Stratton. 1958.

Die Medikamentöse Behandlung der Schilddrüsenerkrankungen. By Professor Dr. W. Grab and Professor Dr. K. Oberdisse. (Pp. 292+viii; illustrated. DM. 39.60.) Stuttgart: Georg Thieme Verlag. 1959.

A Guide to the History of Bacteriology. By T. H. Grainger, Jr. (Pp. 210+xi. $4.50.) New York: Ronald Press Co. 1958.

Television and the Child. An Empirical Study of the Effect of Television on the Young. By Hilde T. Himmelweit, A. N. Oppenheim, and Pamela Vince. (Pp. 522+xix. 42s.) London: Oxford University Press, for Nuffield Foundation. 1958.

Antibiotics Monographs. No. 8. Chloromycetin (Chloramphenicol). By T. E. Woodward, M.D., and C. L. Wisseman, Jr., M.D. (Pp. 159+xiv; illustrated. $4.) New York: Medical Encyclopedia, Inc. 1958.

Antibiotics Monographs. No. 9. Penicillin. By H. L. Hirsh, M.D., and L. E. Putnam, M.D. (Pp. 148+xi; illustrated. $4.) New York: Medical Encyclopedia, Inc. 1958.

Antibiotics Monographs. No. 10. Streptomycin and Dihydrostreptomycin. By L. Weinstein, Ph.D., M.D., and N. J. Ehrenkranz, M.D. (Pp. 116+xi; illustrated. $4.) New York: Medical Encyclopedia, Inc. 1958.

Antibiotics Monographs. No. 11. Modern Chemotherapy of Tuberculosis. By R. S. Mitchell, M.D., F.A.C.P., and J. C. Bell, M.D., M.S., F.A.C.P. (Pp. 109+viii; illustrated. $4.) New York: Medical Encyclopedia, Inc. 1958.

Milestones in Modern Surgery. By A. Hurwitz, M.D., and G. A. Degenshein, M.D. (Pp. 520+xvii; illustrated. £5 12s. 6d.) London, Toronto, Melbourne, Sydney, and Wellington: Cassell and Co. Ltd. 1958.

Tumors and Tumorous Conditions of the Bones and Joints. By Henry L. Jaffe, M.D. (Pp. 629; illustrated. £6 15s.) London: Henry Kimpton. 1958.

Klinische Methoden der Blutgerinnungsanalyse. By J. Jürgens and F. K. Beller. (Pp. 391+xvii; illustrated. DM. 56.) Stuttgart: Georg Thieme Verlag. 1959.

Cholesterol. By D. Kritchevsky. (Pp. 291+ix; illustrated. 78s.) New York: John Wiley and Sons, Inc.; London: Chapman and Hall. 1958.

Paracelsus. An Introduction to Philosophical Medicine in the Era of the Renaissance. By Walter Pagel. (Pp. 368+xii; illustrated. Sw.Fr. 70.) Basel, New York: S. Karger. 1958.

Clinical Endocrinology. By K. E. Paschkis, M.D., E. Rakoff, M.D., and A. Cantarow, M.D. 2nd ed. (Pp. 941+xii; illustrated. £6 15s.) London, Toronto, Melbourne, Sydney, and Wellington: Cassell and Co. Ltd. 1958.

Treatment of Breast Tumors. By R. S. Pollack, M.D., F.A.C.S. (Pp. 147; illustrated. 45s.) London: Henry Kimpton. 1958.

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EXTRACORPOREAL CIRCULATION

A recent report[1] in this *Journal* by a team of workers at the Postgraduate Medical School represents a milestone in this country in the history of operations which can be performed only with the help of a heart-lung bypass machine. This paper, by W. P. Cleland and his colleagues, is on the treatment of ventricular septal defect, and it describes the first series of any size reported in Great Britain. The results clearly show that the machine developed over many years by D. G. Melrose[2] in London can satisfy the requirements of heart-lung bypass quite as well as machines in use in other countries. Although work on heart-lung bypass machines was started as long ago as 1937 by J. H. Gibbon[3] and continued by T. L. Stokes and Gibbon[4] and by C. Dennis and his colleagues,[5] it is only in the last four years that these machines have come into successful and reliable clinical use. The results reported by J. W. Kirklin and his co-workers[6] from the Mayo Clinic and H. E. Warden and his colleagues[7] from Minneapolis have encouraged other surgeons, and now every major centre for cardiac surgery finds it necessary to have one or other of the heart-lung machines available, and reports on the treatment of series of patients are appearing with increasing frequency.[8] The rate of progress in Britain has of necessity been dependent on the allocation of staff, equipment, and money to forward research in this field. However, nearly every major thoracic unit in Britain is now working with one or other of the machines, and their clinical use has started or is about to start in most of them.

By far the most important part in developing the successful clinical application of these machines is the training of a competent team. Operations which require the use of the heart-lung bypass are not and never can be a "one-man show." The surgeons, anaesthetists, and pump operators must all work together from the start in the experimental laboratory.[9] Only when the whole team knows what to do in any given emergency should they consider perfusing a patient. As experience of perfusion grows and the difficulties are successfully met, the whole procedure may become more straightforward, but no substitute for good team-work can possibly be devised. This is underlined by the fact that the variety of successful machines in use throughout the world is now quite large, but it is always the centres with the thoroughly trained teams that achieve the best results. An idea of the number of people necessarily included in a team at one centre is given by the list of Cleland's co-authors, eleven in all.

Success depends on three main conditions. The first is accurate diagnosis. The second is the employment of the correct surgical technique for treating the known defect, and also the ability to correct hidden and undiagnosed abnormalities, such as the patent ductus arteriosus mentioned by Cleland and his colleagues as a silent but relatively common coexisting lesion with a ventricular septal defect. The third condition necessary for success is the ability to carry out a successful perfusion not only under ideal conditions but, more important, when some difficulty such as unexpected haemorrhage complicates the issue. It is this last which makes the pump operator such an important member of the team. The surgeon is fully occupied during perfusion in dealing with the heart itself, and he must feel confident that his pump operator can maintain a satisfactory equilibrium and take the necessary decisions without adding to the surgeon's burden. It may be that highly trained technicians will eventually undertake this work, as they do already in one or two centres, but most units prefer the responsibility to be carried by a doctor with special training. The function of the anaesthetist is as important, or more so, in perfusion as in any other chest operation, and he must maintain the closest liaison with the pump operator, particularly in so far as the maintenance of a steady blood volume and the administration of intravenous fluids and drugs are concerned. The presence of a cardiologist as a member of the team in the operating theatre is highly desirable. Biochemists and haematologists, in reporting on changes in blood chemistry and in preparing blood for perfusion, also play a vital part in the success of an operation.

For an operation on an adult about 16 pints (9 litres) of blood will be required during the perfusion and in the post-operative period. This of itself is going to raise fresh problems for the blood transfusion service when perfusion becomes a common procedure. The storage of blood in plastic bags may prove helpful. I. W. Brown and W. W. Smith[10] have devised a new anticoagulant preservative mixture, and

[1] Cleland, W. P., *et al.*, *Brit. med. J.*, 1958, **2**, 1369.
[2] Melrose, D. G., *et al.*, ibid., 1953, **2**, 57 62.
[3] Gibbon, J. H., *Arch. Surg.* (*Chicago*), 1937, **34**, 1105.
[4] Stokes, T. L., and Gibbon, J. H., *Surg. Gynec. Obstet.*, 1950, **91**, 138.
[5] Dennis, C., *et al.*, *Ann. Surg.*, 1951, **134**, 709.
[6] Kirklin, J. W., *et al.*, *J. thorac. Surg.*, 1957, **33**, 45.
[7] Warden, H. E., *et al.*, ibid., 1957, **21**, 33.
[8] Gerbode, F., *et al.*, *Lancet*, 1958, **2**, 284.
[9] Drew, C. E., *et al.*, *Brit. med. J.*, 1957, **2**, 1323.
[10] Brown, I. W., and Smith, W. W., *Ann. intern. Med.*, 1958, **49**, 1035.
[11] Bahnson, H., *Extracorporeal Circulation*, 1958, Springfield, Illinois.

suggest that when this is used blood can be drawn three to five days before perfusion and, if suitably heparinized, used in the pump; but it will also last two weeks if stored for use as ordinary transfusion blood.

The selection of cases for surgical treatment with the use of a pump oxygenator is a matter for the most careful investigation by the cardiologist, who will require all the information that can be given by such techniques as cardiac catheterization and angiocardiography. As Cleland and his colleagues point out, the height of the pressures on the right side of the heart and evidence of increased pulmonary vascular resistance, which can lead in some cases to reversal of the shunt, have to be taken into consideration before an operation to correct a septal defect is decided upon. In the most severe cases of pulmonary hypertension and increased pulmonary resistance surgery at present has a high operative mortality. Published reports show that the best results with the heart-lung bypass are obtained in the correction of atrial and ventricular septal defects and that these should if possible be treated in childhood before any serious strain on the heart has developed owing to the shunts. The curative correction of Fallot's tetralogy is possible only by the use of a pump oxygenator, but the operative mortality is still high even in the most experienced hands. No team should attempt this operation until it has been thoroughly trained in perfusion technique and has gained experience in the repair of the simpler defects. Almost every other congenital heart lesion may be open to radical cure, or at least improvement, by this technique, and as knowledge is gained even the difficulty presented by transposition of the great vessels should be overcome. In the surgical treatment of acquired valvular disease, particularly mitral incompetence and aortic stenosis and regurgitation, no fully satisfactory operations have yet been developed, and the advent of cardiopulmonary bypass may enable much more progress to be made. The major difficulty here that a pump oxygenator does not overcome is that of gross destruction of valve tissue. Much experimental work is being devoted to the fabrication of prosthetic valves: with the co-operation of manufacturers physiologically satisfactory valves may soon be available, and their insertion in the correct position becomes a practical proposition with the use of extracorporeal circulation.

The preparation of a machine for perfusion has to be undertaken with the greatest care. The most exacting cleanliness and sterility are vital, and experience has taught perfusion units to use fresh materials so far as possible each time and to clean the rest with strong solutions of caustic soda to remove any persisting fibrinoid deposit.[11] The effect of pump-oxygenators on the blood circulating through them still needs study, and although post-perfusion bleeding steadily decreases in all units with increasing practice it remains a major source of worry. Brown and Smith[9] discuss the influences that may encourage bleeding and suggest that the extracorporeal heart-lung circuit may activate systemic coagulation through liberation of thromboplastic substances and thus exhaust essential clotting factors. While haemolysis due to mechanical fracture of red cells in the machine does occur, it is not sufficiently severe to cause trouble; but the survival of red cells after perfusion does appear to be shortened in some cases. Brown and Smith put forward the theory that circulation through the pump oxygenator may enhance in some way certain red-cell antigens, so that antibodies to them are provoked when these cells reach the circulation of susceptible recipients.

Since the heart-lung bypass is quickly becoming a standard clinical method in centres where cardiac surgery is undertaken, a decision may soon be needed on how many centres for this work the country needs and can afford. Very relevant to this decision are the numbers of patients suitable for operation now, and the numbers likely to present in the future when all those on the initial waiting-lists have been treated.

ENDEMIC GOITRE

Goitre occurs with varying intensity in almost every country in the world: it is seen in those who live in the heat of the tropics and in those who inhabit the icy wastes around the Poles. The most severe endemics of goitre are in high mountain regions—the slopes of the Himalayas, the Swiss Alps, and the Cordillera of the Andes being probably the best-known examples. However, goitre also occurs in low-lying areas, such as the Netherlands, and is often found near the sea as well as inland. A recent issue of the *Bulletin of the World Health Organization* has been devoted to this subject, and the opening article by F. C. Kelly and W. W. Sneddon[1] provides the best account of the prevalence and geographical distribution of endemic goitre which has so far appeared. Their long review brings knowledge of this subject fully up to date, providing almost a thousand references to the literature.

Largely as a result of the pioneer work of Sir Robert McCarrison in India much is now known about simple goitre, but much still remains to be discovered. Geochemists point out that the type of terrain in which goitre abounds is that which has been subjected to flooding or glaciation and from which most of the iodine has

therefore been washed out and carried away to the sea. Thus, where the iodine content of the soil is low, the iodine intake of the people will be likewise inadequate and goitre results. The poorer the people the more directly dependent will they be upon the soil on which they live, and under such conditions the endemic may be severe. But when people prosper they import food from outside the district in order to give variety to the diet and so obtain a modicum of iodine. Thus very often the size of a goitre is a good indication of the income of the individual.[2]

The complications of endemic goitre are reviewed by F. W. Clements,[3] who is well known for his work in Australia and Tasmania. He points out that hypothyroidism is often difficult to detect in endemic areas, for its onset is gradual and overt myxoedema does not usually arise. In addition to marshalling the evidence that the incidence of hyperthyroidism is greater in these areas, he reviews the relationship of carcinoma of the thyroid to simple goitre, and pays particular attention to the subject of cretinism, classifying it according to the plan suggested by J. B. Stanbury and A. Querido.[4] The technique of carrying out a goitre survey has been well established in the past, and the principles to be observed are clearly laid down in this symposium by a team working in Guatemala.[5]

It should be remembered that many factors may influence the distribution of goitre as well as the all-important one of a low intake of iodine. Clements[6] has incriminated the milk from cows fed on kale; this is said to have been responsible for an epidemic of goitre in schoolchildren in Tasmania. Kale contains a goitrogen, vinyl-thio-oxazolidone,[7] which is excreted in the milk. Raymond Greene and his co-workers[8] at New End Hospital have, however, not been able to confirm this with kale-fed cows in England. Recent reports that there had been an epidemic of goitre in the Multan area of West Pakistan since its partition from India attracted attention in the press. This outbreak was investigated by Margaret Murray and Dagmar Wilson and colleagues,[9] who found that the probable cause was the low iodine content of the water in the local wells. Another factor which may increase the endemicity of goitre is the presence of fluorine, and D. G. Steyn[10] has shown that this halogen is particularly rich in the soil and water of south-west South Africa. Likewise calcium has been known since the last century to be goitrogenic, and when the water is hard or the subsoil rich in limestone, as for example in Derbyshire, enlargement of the thyroid is more common.[11 12]

On the important subject of the prevention of goitre J. Matovinovic, of Jugoslavia, and V. Ramalingaswami[13] give authoritative advice, outlining what has been accomplished since prevention was first put on a rational basis forty years ago with the introduction of iodized salt by D. Marine and O. P. Kimball.[14] The daily intake of iodide, in their view, should not be higher than 200–300 microgrammes, and the simplest way of giving it to most people is still to add it to the salt. For children, iodide may be used in the manufacture of sweets, and in certain parts of the world where salt is prepared locally iodide can be introduced into flour. Many countries have already introduced iodized salt and are now beginning to reap the benefits of it; these include Switzerland, New Zealand, Jugoslavia, and some of the South American nations. Great Britain has still not taken this step, and many think that it is long overdue. Forty years ago Marine stated: "Simple goitre is the easiest of all known diseases to prevent. It may be excluded from the list of human diseases as soon as society determines to make the effort."

[1] Kelly, F. C., and Sneddon, W. W., *Bull. Wld Hlth Org.*, 1958, **18**, 5.
[2] Stanbury, J. B., *et al.*, *J. clin. Endocr.*, 1952, **12**, 191.
[3] Clements, F. W., *Bull. Wld Hlth Org.*, 1958, **18**, 175.
[4] Stanbury, J. B., and Querido, A., *J. clin. Endocr.*, 1956, **16**, 1522.
[5] Perez, C., *et al.*, *Bull. Wld Hlth Org.*, 1958, **18**, 217.
[6] Clements, F. W., *Med. J. Aust.*, 1955, **2**, 369.
[7] Greer, M., *et al.*, *Endocrinology*, 1948, **43**, 105.
[8] Greene, C. R., *et al.*, *J. Endocr.*, 1958, **17**, 272.
[9] Murray, M., *et al.*, *Trans. roy. Soc. trop. Med. Hyg.*, 1958, **52**, 223.
[10] Steyn, D. G., *et al.*, *Endemic Goitre in the Union of S. Africa and Some Neighbouring Territories*, 1955. Pretoria.
[11] Boussingault, J. B., *Ann. clin. Phys.*, 1831, **48**, 41.
[12] Taylor, S., *J. clin. Endocr.*, 1954, **14**, 1412.
[13] Matovinovic, J., and Ramalingaswami, V., *Bull. Wld Hlth Org.*, 1958, **18**, 233.
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THE HAEMOLYTIC REACTION

The use of tracer amounts of radioactive chromium, ^{51}Cr, as a label for red cells has greatly facilitated research into mechanisms of haemolysis. By this technique it has become possible to measure the life-span of a patient's red cells in his own circulation (which was not possible by the Ashby method of differential agglutination), and by counts made over the surface of the body to discover the main sites of haemolysis.[1 2] Where this is due to an antigen–antibody interaction the method has enabled the rate and site of red-cell destruction to be correlated with the type of antibody. Briefly, it has been found that strongly or coarsely agglutinated cells are trapped and destroyed in the liver and lungs, while weakly or finely agglutinated cells are mainly filtered out of the circulation by the spleen.[3 4]

Recently J. H. Jandl and A. S. Tomlinson[5] have reported detailed observations on an interesting side-effect of antigen–antibody reaction—namely, the onset of leucopenia and neutropenia, which, with fever, they consider to be characteristic of the normal

response of the host to immune haemolysis. Although the association of leucopenia with paroxysmal haemoglobinuria was recognized by F. Widal and co-workers[6] in 1913, the phenomenon has until recently not been studied in detail. Jandl and Tomlinson found that when there was anti-A or anti-B incompatibility the injection of 10 ml. of washed incompatible red cells was followed within two to three minutes by a fall in the leucocyte count to about 30% of the control levels, with a subsequent rise to supranormal levels in two to four hours. Differential counts showed that the leucopenia was brought about by the almost complete disappearance of polymorphonuclears and monocytes from the circulation. Mild pyrexia, maximal in three to four hours, followed the injection. However, none of the recipients of the incompatible blood developed rigors, though a few of them experienced transient symptoms, including lumbar pain, dyspnœa, hyperperistalsis, emotional instability, and flushing of the face.

In control experiments it was found that haemolysed compatible red cells or haemoglobin solutions derived from compatible cells could be injected without producing leucopenia or any symptoms, but lysed incompatible cells or A substance produced the same effects as did intact A cells in a recipient whose serum contained anti-A.

Similar observations were made on patients with anti-D in their serum given D+ red cells, though the results were different: there was eventually the same degree of leucopenia and neutropenia, but this took about one hour to reach its maximum. Chills were regularly experienced between 50 and 75 minutes after the injection and were often accompanied by vomiting, and the temperature rose by about 3° F. (2° C.).

In both series of patients the fall in leucocyte count paralleled the disappearance of the red cells from the blood stream. Cortisone and aspirin repressed the rise in temperature but did not affect the degree of leucopenia or the rate of elimination of the incompatible cells. The platelet counts and fibrinogen concentrations of the recipients remained unaltered throughout the experiments.

The effect of damaging red cells by non-immunological means was next investigated. Thus, cells incubated at 37° C. for 4–48 hours or exposed to acetylphenylhydrazine or lecithin were reinjected into the donors. Although these cells had short survival times, neither leucopenia nor systemic effects resulted.

The leucopenia, chills, fever, dyspnœa, flushing, urticaria, gastro-intestinal disturbance, and so on, thus appear to be the consequences of *immune* haemolysis and not of haemolysis itself. Jandl and Tomlinson conclude that all these changes, and probably thrombocytopenia and renal injury also, result from the harmful effects on leucocytes and platelets of released antigen–antibody complexes. They suggest, too, that damage to the cells' surfaces leads to liberation of "endogenous pyrogen," histamine and serotonin, and that they are likely to be among the substances which cause the systemic effects of incompatibility.

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A HAZARD OF PURGATION

One of the hazards of indiscriminate purgation is the heavy loss of electrolytes which accompanies diarrhoea from any cause. The body's stores of sodium or potassium may become severely depleted. This is the subject of an article by Drs. N. F. Coghill, P. M. McAllen, and Felicity Edwards at p. 14 of the *Journal* this week. In two of their three cases regular purgation was the sole cause of the diarrhoea and in the other one it made the patient's existing diarrhoea more severe.

During recent years the importance of maintaining the correct electrolyte balance of the body in illnesses such as ulcerative colitis and idiopathic steatorrhoea has been widely recognized. Potassium depletion is particularly likely to occur in severe diarrhoea and can cause a variety of symptoms such as profound muscular weakness and even actual paralysis, myocardial weakness, intestinal hypotonus going on to paralytic ileus, and alkalosis associated with renal failure.[1] That the simple diarrhoea brought about by purgatives can have the same effect is less well known, though a number of studies have pointed the same moral as that of Coghill and his colleagues. W. B. Schwartz and A. S. Relman[2] described two otherwise healthy women who developed severe potassium depletion because of chronic diarrhoea induced by regular use of laxatives containing aloin. This severe depletion apparently developed gradually over the course of months or years without producing striking symptoms or signs other than malaise, muscular weakness, and abdominal pains. J. M. French and colleagues described two patients with chronic diarrhoea caused by phenolphthalein; steatorrhoea was a feature while the diarrhoeal state was present. B. J. Houghton and M. A. Pears[4] published a case report of chronic potassium depletion due to purgation with cascara, the patient showing severe muscular weakness, anorexia, and vomiting. J. D. Aitchison[5] likewise described a patient suffering from potassium depletion due to excessive use of cascara for several months. The patient presented with muscular weakness, which was

attributed to cerebral thrombosis until a routine electrocardiogram showed changes indicative of hypokalaemia, and this was confirmed biochemically. There was impairment of renal function of a type known to result from potassium depletion,[6] and the function became normal with potassium therapy.

The purgatives most likely to cause these disturbances are those which act as intestinal irritants and thus stimulate the gut to propel its contents faster. Among the vegetable group some agents, such as cascara sagrada and aloes, act chiefly on the large intestine. More potent vegetable purgatives, such as jalap and colocynth, act chiefly on the small intestine, causing increased motility, which is accompanied by reflex hyperactivity of the large bowel. Among the pure chemicals phenolphthalein forms a soluble salt which acts chiefly on the colon, though the small intestine may also be stimulated. Calomel becomes partly converted into mercuric oxide in the small intestine and the mercuric ion has an irritant action. These agents, when used regularly for long periods, can cause demonstrable changes in the *x*-ray appearances of the intestine, simulating those found in enterocolitis.[7] Such changes are said not to occur with the use of saline cathartics or of other agents which operate simply by increasing the bulk of the intestinal contents.

The habit of taking cathartics is so widespread that it is perhaps remarkable that comparatively few patients have been reported to have serious metabolic effects from their use. Possibly more cases will be reported now that attention has been focused on the problem. So far as less serious effects are concerned, specialists in the field of gastro-enterology have long been aware that addiction to purgatives frequently causes bowel dysfunction. For example, 73% of S. M. Jordan's patients with functional disturbances of the colon used cathartics or irritating enemata regularly,[8] while nearly half of those reported by E. N. Collins did so.[9]

It is worth considering how the purgation habit arises. In Western society early bowel training is an accepted feature of infant upbringing, and there is a widespread view that harm will result if defaecation does not occur daily. A subject conditioned to such ideas may possibly experience symptoms such as headache, malaise, and abdominal discomfort if he fails to empty his bowel at his usual time. Consequently he may take a brisk purgative. Most purgatives when taken in full doses cause the large bowel to empty itself completely, whereas with normal defaecation only the sigmoid and descending colon are evacuated. After total evacuation of the large bowel it is normal for two or three days to elapse before the left side of the colon becomes filled with faeces, so that when mass peristalsis occurs the faecal column enters the upper rectum and initiates the defaecation reflex. To the bowel-conscious subject this period of time without a bowel action is too long for his peace of mind, and he is tempted to take more purgatives to cure himself of what he regards as constipation. When this happens a vicious circle sets in.

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CENSUS INNOVATIONS

The 1951 census enumerated in England and Wales the largest population ever to be recorded there—43,757,888 persons. This was almost five times the number enumerated in 1801, when the first of the present series of decennial censuses was held. A general report[1] now published shows that the 1951 enumeration was probably also the most accurate to have been carried out.

Among several innovations was one of notable value—the 1% sample tables. They were published only a year after the census was held and gave many estimates of importance to governmental administration and public health. It has since been possible to test the validity of these estimates, with certain reservations, against the figures for the whole population from which the samples were drawn (an opportunity usually denied to statisticians). They stand up to the test well, and the sampling errors were no more than might have been expected on theoretical grounds. The experiment is clearly worth repeating, for it has been helpful in overcoming one of the characteristic difficulties of our time—namely, interpreting quickly enough the mass of data that have to be gathered for the efficient government of a complex and densely populated nation.

For the first time the census form included questions on whether the household had exclusive use of, or shared with another household, or entirely lacked certain domestic and sanitary arrangements. These comprised a piped water supply, a cooking stove, a kitchen sink, a water-closet, and a fixed bath. Just over half the households of England and Wales were recorded as having exclusive use of them. The proportion was 59% for households in undivided dwellings but only 10% for households in shared dwellings. Out of 13 million private households 6.8 million had exclusive use of all five arrangements, 11.3 million of stove and sink, 10.6 million of piped water supply to the house, and 10.3 million of a water-closet.

Whether a person lives in an urban or rural area has lately been recognized more precisely as affecting his health and expectation of life. The air polluted by smoke in this century has its parallel as a public health problem in the water polluted by bacteria 100 years ago. If causes of mortality are to be accurately understood, it is clearly helpful to define with precision what the boundaries and population of an urban area are, though smoke pollution to some extent must cause trouble

[1] *Census 1951, England and Wales, General Report*, H.M.S.O., 13s.

beyond these boundaries. Analysis by type of administrative area, such as county borough, urban district, and rural district, has been found not to give a clear index of urban development. A new definition was therefore devised. A district was considered to be urban when it came within density categories 1 and 2 of the Ministry of Housing and Local Government. On this basis the urban population amounted to about 32 million and the rural to about 12 million; and over half of the country's total population is found by this method to be living in cities of over 100,000 population. Specifically urban causes of ill-health are thus seen to be of moment to a great many people.

SULPHONAMIDE MIXTURES

The precipitation of sulphonamides in the renal tract is a troublesome and sometimes dangerous side-effect of administering this group of drugs. D. Lehr[1 2] has shown that the sulphonamides, even if closely related chemically, are soluble in water in one and the same solution almost to the extent of their separate solubilities. In experiments on rats he found that, with doses of 1.5 g. per kg. body weight, the percentage mortality with single sulphonamides varied between 85 and 52%, whereas doses of 1.5 g. per kg. made up of various mixtures of sulphonamides caused no deaths. A. R. Fisk and colleagues[3] confirmed these findings, and showed that over the *p*H range likely to be found in urine the solubility of a mixture of equal parts of sulphathiazole, sulphadiazine, and sulphamerazine was greater than the most soluble alone, this being true for the drug itself and for the acetylated compound. Furthermore, when this mixture was given to rabbits in doses of 1.0 g. per kg. no renal calculi were formed, whereas the same dose of a single sulphonamide always resulted in a calculus.

The antibacterial efficiency of sulphonamide mixtures is the subject of some debate. Lehr[1] found that *in vitro* their full therapeutic efficiency was retained. The subject has also been investigated by F. B. Schweinburg and A. M. Rutenburg,[4] and L. Weinstein and E. B. Murphy[5] used sulphadimidine, sulphadiazine, sulphamerazine, and sulphathiazole, alone and in various mixtures, and tested their effectiveness *in vitro* against a wide range of Gram-positive and Gram-negative organisms. They found that the effectiveness of mixtures of sulphonamides was unpredictable; sometimes the mixture had an additive or even a potentiating effect and sometimes the mixing of sulphonamides appeared to depress antibacterial activity. Schweinburg and Rutenburg recommend that "the use of sulphonamide mixtures in preference to a single effective sulphonamide is justified only when *in vitro* sensitivity tests demonstrate for the components of the mixture either an additive or potentiating effect." In clinical trials sulphonamide mixtures seem to give favourable results. Lehr[6] reported 170 unselected patients with a variety of infections in which clinical results were satisfactory and the incidence of side-effects was low.

In experiments to discover the most effective mixture, Lehr[6] found that sulphadiazine and sulphamerazine combined with either sulphathiazole or sulphacetamide were the best mixtures, combining a high clinical effectiveness with a low toxicity. Later, sulphathiazole, which was perhaps the most toxic of the three, was replaced by sulphadimidine. In practice a number of preparations of sulphonamide mixtures are available. The tab. trisulphon. (*B.N.F.*) contain sulphadiazine 0.185 g., sulphathiazole 0.185 g., and sulphamerazine 0.130 g. This would appear to be a useful mixture, as each of the three sulphonamides has a high antibacterial activity; the quantity of sulphamerazine is lower than that of the other two drugs because it was found to be more apt to give rise to urinary crystals. Other preparations contain sulphadiazine, sulphadimidine, and sulphamerazine, or sulphadiazine, sulphamerazine, and sulphacetamide. Absorption of such mixtures is satisfactory, resulting in adequate levels of the drugs both in the blood and in the cerebrospinal fluid.[7–9]

The possibility of an increased risk of drug sensitivity to several sulphonamides which might follow the use of mixtures has been raised.[10 11] Lehr[6] has pointed out that the incidence of sensitization reactions ran parallel with the dose of the sulphonamide employed. He considered that the low dosage of individual sulphonamides which were used in sulphonamide mixtures might well reduce the frequency of sensitivity reactions, and this was substantiated by his experience with 700 patients treated with such mixtures.

Though the evidence suggests that sulphonamide mixtures had advantages over the less soluble sulphonamides when used alone, it seems rather doubtful if this holds for the more recently introduced drugs in this group. Long-term toxicity experiments on animals, in which large doses of two sulphonamide mixtures containing sulphadiazine, sulphathiazole, and sulphamerazine and sulphadiazine, sulphamerazine, and sulphadimidine were compared with sulphafurazole, showed that the last drug alone was less toxic than the mixtures, though this could perhaps be partially explained by the fact that the blood level of sulphonamides is rather higher after the mixture than the single drug.[12] There is not yet any direct evidence comparing the toxicity and effectiveness of sulphadimidine with that of sulphonamide mixtures, but it seems unlikely that the mixtures would have any advantage over sulphadimidine alone.

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Drug Treatment of Disease

DIURETICS

BY

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Strictly speaking, any substance that increases the output of urine is a diuretic, but in therapeutics the term is usually applied to compounds which are used in the treatment of oedema. Since oedema fluid is composed largely of water, sodium, and chloride, an effective diuretic must enhance the renal excretion of all these constituents. Over the years a great many diuretic agents have been introduced, but little would be gained by reviewing them all or discussing those which have only a limited use in special circumstances. Rather this is an account of those compounds which to-day are of most general value and most widely used.

Pride of place must be given to mersalyl and similar organic mercurial compounds, which, given parenterally, have been for many years the sheet anchor in the relief of oedema. Only within recent months has the position of mersalyl been seriously challenged. The newcomer is chlorothiazide ("saluric"), a non-mercurial compound with the great advantage of being effective by mouth and having an equivalent potency. In addition there are other less potent substances, unsuitable for the initial treatment of serious oedema but of value in preventing the reaccumulation of oedema fluid or for the relief of less serious oedematous conditions. Three of these compounds—ammonium chloride, aminophylline, and acetazolamide ("diamox")—are mainly used to potentiate the action of mercurial diuretics and to prevent the development of electrolyte imbalances.

Pharmacology

Diuretics can be divided into three main groups according to the mechanism by which they increase the urinary output. First are compounds, such as aminophylline, which increase the blood supply to the kidneys and thereby increase the amount of water and solutes filtered by the glomeruli. Aminophylline has only a transient diuretic action, but by increasing renal blood flow may potentiate the effects of mersalyl in refractory patients if given in a dose of 0.5 g. intravenously two hours after the injection of mersalyl.

Second are those substances which induce an osmotic diuresis by impeding the reabsorption of water in the renal tubules. Urea is an example of this type, but is seldom used because of its unpalatability.

The third, and by far the most important, group are those compounds which directly or indirectly depress the reabsorption of sodium. Normally a large proportion of the sodium ions filtered through the glomeruli are returned to the blood stream through the tubular cells. In diseases which give rise to oedema an even greater proportion of the glomerular filtrate is reabsorbed, and the excessive retention of sodium, chloride, and water is responsible for the development of oedema. If the reabsorptive activity of the tubular cells for sodium is diminished, more sodium is excreted and carries with it an increased amount of water. The exact mechanism by which this is achieved varies with the different members of the group.

Mersalyl impedes the reabsorption of chloride ions, which are excreted in increased amounts, taking with them sodium ions and water. Slightly more chloride than sodium is eliminated, and, if the treatment is too frequent or prolonged, chloride depletion and a fall in the serum chloride level develop. As a result less chloride is filtered through the glomeruli, and the effect of mersalyl is lost. Thus, despite continuing oedema, the patient becomes unresponsive. *Ammonium chloride*, given two hours before the mersalyl injection in the form of two 0.5 g. enteric-coated capsules, prevents the development of mercurial refractoriness by providing chloride ions and also has a diuretic action in its own right.

Chlorothiazide has in many respects an action similar to mersalyl, but the tendency to hypochloraemia is less marked, and seldom occurs in patients with a normal moderately restricted intake of sodium chloride. On the other hand chlorothiazide has a greater tendency to enhance potassium excretion, perhaps because of its additional mild carbonic-anhydrase inhibitory action. Potassium depletion may occur in debilitated patients with a poor appetite, and hence a low potassium intake, who avidly retain sodium and need chlorothiazide more frequently than twice a week. Hypokalaemia is usually asymptomatic but may cause malaise, apathy, weakness, and loss of deep tendon reflexes. It may precipitate neuropsychiatric disturbances in patients with portal cirrhosis, and increases the sensitivity of the heart to digitalis. Thus a fully digitalized patient when given chlorothiazide may develop anorexia, nausea, and vomiting, with undue slowing of the pulse rate and the occurrence of ventricular extrasystoles—manifestations which call for a reduction in the dose of digitalis.

Potassium depletion can be prevented by encouraging a high intake of potassium in the form of tinned pineapple juice, fresh or tinned orange juice, salt-free "marmite," blackcurrant juice, or burgundy. If chlorothiazide has to be given more often than twice weekly for several weeks on end, the dietary intake of potassium must be supplemented, preferably with a mixture of potassium chloride, because tablets or capsules may not disintegrate in the intestinal tract. A palatable mixture to be taken three or four times a day is:

R	Potassium chloride	.. 1 g.
	Syrup simplex	.. 2 ml.
	Alcohol (95%)	.. 2 ml.
	Raspberry flavouring	q.s.
	Chloroform water to	15 ml.

If chlorothiazide is given daily, potassium chloride should also be given daily. If chlorothiazide is given on three days a week, potassium chloride is taken on the other four days.

Aminoisometradine ("rolicton") also increases the renal excretion of sodium and chloride in approximately equal proportions, but, being less potent than either chlorothiazide or mersalyl, is less apt to cause electrolyte disturbances. It cannot be recommended for the initial

treatment of severe oedema, but finds a place in maintenance therapy.

Acetazolamide has a different action from the other compounds. It is an inhibitor of carbonic anhydrase and impedes the reabsorption of bicarbonate ions by the renal tubules. The bicarbonate is excreted in company with sodium, potassium, and water but little chloride. After a short time a metabolic acidosis (low serum bicarbonate and high chloride level) develops, and, because fewer bicarbonate ions are filtered through the glomeruli, acetazolamide becomes progressively less effective. It is not potent enough to be of clinical value in the initial treatment of oedema, nor can it be relied upon to prevent the reaccumulation of oedema fluid, but it is of value as an adjuvant to mersalyl because it may prevent the development of hypochloraemic alkalosis.

Chlormerodrin ("mercloran") is an oral organic mercurial compound which is sometimes of value in keeping ambulant patients, who have recovered from congestive failure, free of oedema. The smallest effective dose should be given, but even then diarrhoea may occur.

Potency

Some indication of the relative potency of the different diuretic agents is given in Tables I and II. The comparison is based on the increase in sodium excretion induced by a maximally effective single dose, and the results are expressed as a percentage of the sodium diuresis following 2 ml. mersalyl, which is taken as 100%.

Indications

Oedema due to cardiac, renal, or hepatic disease constitutes the most important indication for diuretic therapy. The fluid retention may be confined to the legs or sacrum, or be localized to the peritoneal or pleural cavities as ascites or a hydrothorax. It may also be limited to the lungs in left-sided heart failure, and be responsible for paroxysmal nocturnal dyspnoea ("cardiac asthma"). In these circumstances the renal retention of sodium is often avid, and only one or other of the two most potent diuretics—chlorothiazide or mersalyl—is likely to be effective. To some extent diuretics are only symptomatic treatment, and in every instance appropriate measures to improve the underlying disease process must be instituted too. In some instances severe restriction of sodium intake is necessary, but most patients prefer to continue taking a diuretic and eat palatable salt-containing food rather than have a salt-free diet and no diuretic.

Diuretics are not indicated for the relief of the mild oedema in acute glomerulonephritis, but may add greatly to the comfort of the nephrotic patient with anasarca or the patient with chronic glomerulonephritis in whom oedema may be due to the renal disease or to superimposed hypertensive cardiac failure. In general, aspiration of ascites or hydrothorax is unnecessary and should be avoided because the protein content of the fluid is lost from the body.

In other conditions which call for diuretic therapy sodium retention is often less avid and the volume of oedema fluid is smaller. Oedema may develop in association with obesity; in the premenstrual syndrome, when there may be a sudden weight gain of 6 to 10 lb. (2.7–4.5 kg.) seven to ten days before menstruation begins; during administration of cortisone or hydrocortisone but less commonly with prednisone or prednisolone; and in patients who need massive doses of oestrogens to control a prostatic carcinoma. Diuretics, particularly chlorothiazide, are of value in the treatment

TABLE I.—*Initial Treatment of Cardiac, Hepatic, or Renal Oedema*

Drug	Route	Toxic Manifestations	Electrolyte Disturbances	Potency (see Text)	Dosage		Adjuvant Therapy
					Per Day	Frequency	
Chlorothiazide	Oral	Very uncommon. Rash. Anorexia. Malaise	Hypokalaemia causing digitalis intolerance, and in cirrhotics neuropsychiatric disturbances. Hypochloraemia	100%	1 g. twice daily	(*a*) Tuesdays and Fridays (*b*) Mondays, Wednesdays, and Fridays (*c*) Daily	None if appetite good and potassium intake (fruit-juice) is high Potassium chloride supplements of 2–6 g. daily on Tuesdays, Thursdays, and Saturdays Potassium chloride supplements daily
Mersalyl	Intramuscular	Very uncommon. Pain at site of injection. Rashes. Fever. Malaise. Diarrhoea. Stomatitis. Ventricular fibrillation	Hypochloraemia causing unresponsiveness. Hypokalaemia. Hyponatraemia	100%	2 ml.	(*a*) Tuesdays and Friday (*b*) Mondays, Wednesdays, and Fridays	Ammonium chloride 1 g. in capsules 2 hours before each injection In refractory cases 0·5 g. aminophylline intravenously 2 hours after mersalyl injection

TABLE II.—*Maintenance Therapy or Treatment of Mild Oedema*

Drug	Route	Toxic Manifestations	Electrolyte Disturbances	Potency (See Text)	Dosage		Adjuvant Therapy
					Per Day	Frequency	
Chlorothiazide	Oral	As above	As above	100%	0·5–1·0 g. twice daily	Twice or thrice weekly	Potassium chloride supplements of 2–6 g. on non-chlorothiazide days, in patients with cardiac or liver disease
Aminoisometradine	Oral	Nausea, vomiting, diarrhoea. Dizziness, tinnitus, deafness. Rashes	Hypochloraemia	70%	400 to 800 mg. (1–2 tablets)	Daily	—
Chlormerodrin	Oral	Nausea, diarrhoea, stomatitis, colic. Dermatitis	None reported	50%	1 to 4 tablets	Daily or alternate days	—
Acetazolamide	Oral	Drowsiness. Malaise. Headaches. Paraesthesiae	Acidosis. Hypokalaemia	25%	250 to 500 mg. (1–2 tablets)	Daily for 5 days	—

of pre-eclamptic toxaemia. The loss of oedema may be accompanied by a reduction in blood pressure, but despite the improvement in the mother the outlook for the baby is not materially better.

Diuretics are of little value in the relief of lymph-oedema, oedema due to varicose veins or venous obstruction, or the puffiness of the ankles many women experience after standing on a hot day.

Choice of Diuretic and Dosage

In the initial treatment of oedema due to cardiac, renal, or hepatic causes either chlorothiazide or mersalyl may be given. A preliminary test dose of 0.5 ml. mersalyl should always be given. If there are no untoward reactions (rigor, nausea, vomiting, pain at the injection site, or rash), the full dose of 2 ml. is given intramuscularly twice (rarely thrice) weekly, being preceded by 1 g. ammonium chloride or 250–500 mg. acetazolamide to prevent the development of hypochloraemia. The injection should always be intramuscular, because a number of sudden deaths due to ventricular fibrillation have been recorded after intravenous administration. Although mersalyl may theoretically damage the renal tubules, in practice this is very rare unless excretion is delayed. Thus proteinuria is not a contraindication to its use, but a blood urea in excess of 100 mg. per 100 ml. is.

Chlorothiazide is as potent as mersalyl in most patients, and the ease of oral administration and the flexibility of dosage allows treatment to be readily adjusted to the patient's individual needs. Indeed, there is a temptation for too frequent dosage. The optimal daily dose is 2 g. (1 g. being given at 8.30 a.m. and 1 g. at 2 p.m.). As shown in Table I, the frequency of dosage can be varied to the needs of the patient. Twice or three times a week is often sufficient, but more seriously ill patients may require treatment every day. If chlorothiazide has to be given more often than twice a week, a supplement of potassium should be given as laid down in Table I. Not only does this help to prevent any tendency to hypokalaemia but it is valuable for replacing the potassium stores, which are often depleted in consequence of the metabolic disturbances that accompany cardiac and hepatic failure.

Maintenance Therapy

In cardiac, renal, or hepatic oedema initial treatment is continued until evidence of oedema has gone, and the diuretic response, as judged by daily changes in the patient's weight, has largely ceased. This usually takes two or three weeks, and then it may be possible to stop diuretics altogether. Not infrequently, however, there is an increase in weight and recurrence of mild oedema, so that maintenance therapy becomes necessary. The patient prefers drugs administered by mouth, and four, arranged in order of relative potency, are listed in Table II. Chlorothiazide is more effective than the others, which may fail to prevent the reaccumulation of oedema fluid. The action of acetazolamide is self-limiting, and if the dose of chlormerodrin is increased diarrhoea often follows. The frequency and dose of chlorothiazide can be adjusted to the patient's needs, but, if given more often than twice weekly, potassium supplements as indicated in Table II must be given too. The duration of treatment can be judged only by the patient's response, but in cardiac and hepatic diseases and often in renal conditions diuretics may be necessary for the rest of the patient's life.

The same methods of treatment can also be used for the initial treatment of conditions which cause a milder degree of oedema. In premenstrual oedema, the diuretic is started as soon as the symptoms develop—usually 5–10 days before the period—and continued until menstruation is well established. In pre-eclamptic toxaemia treatment is continued until delivery, and in patients with steroid-induced oedema diuretics are often required until the steroid therapy is reduced or stopped.

DECORATION OF THE ANAESTHETIC ROOM: A STUDY OF PATIENTS' REACTIONS

BY

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Originating as a small annexe to the theatre, the anaesthetic room has evolved into an integral part of the operating-block. Unfortunately it has tended to acquire the coldly utilitarian lines of the theatre, and frequently is too small. The necessary floor space has been recommended as 140 sq. ft. (13 sq. m.) (Ministry of Health, 1937) and as 196 sq. ft. (18.2 sq. m.) (Ward, 1949). The new anaesthetic room at the Chelsea Hospital for Women occupies 216 sq. ft. (20 sq. m.), and this may be reasonably regarded as the minimum space necessary for modern anaesthetic techniques.

Steps taken to relieve the austerity of the room have been discussed. Ostlere (1950) recommends that the room should be divided by a curtain, with the necessary apparatus concealed behind it so that the patient does not see it. Hewer (1955) describes a painting of a soothing and tranquil nature on the wall and ceiling of the anaesthetic room.

The value of such steps is hitherto unestablished, since it rests on two unproved assumptions. Firstly, that all or most of the patients on arrival at the anaesthetic room are sufficiently awake to see and be conscious of their surroundings. Secondly, that, if so, they are in any way appreciative of or influenced by them. The trouble and expense involved are wasted if the patients are all asleep or, alternatively, are totally indifferent to their surroundings. The object of this paper is to discuss the aims of such decorations and to assess their value by observation and questioning of a sample of patients who have been through the new and decorated anaesthetic room at the Chelsea Hospital for Women.

Aims of Schemes of Decoration

At first it might reasonably be supposed that the aim should be to exert a soporific effect on the patient and so enhance the effect of the premedication, such a painting being of the nature of that described by Hewer (1955). Alternatively, it may quite feasibly be thought that, if the drugs used for premedication have not succeeded in making the patient sleepy, it is unlikely that any form of decoration will be able to repair this deficiency. Thus, what is needed is something to amuse

and distract the mind of the patient whose sharpened degree of apprehension has been such as to vitiate the effect of the opiate. This happily allows of a wide choice and variation of subject matter of any painting or form of decoration.

Lighting and Decoration of the Anaesthetic Room of the Chelsea Hospital for Women

With the exception of three overhead lights in a recessed portion, and one spotlight for emergency use, all the lighting is indirect and is thrown from two battens on the walls up on to the picture, which is painted on the ceiling and occupies the greater part of it (Fig. 1). The subject of this picture is a composite farm scene (Fig. 2), the treatment being in the nature of a gentle and light-hearted parody. Sheep are jumping over a fence ; pigs are peering over their pens ; the cows are being driven home ; and various other activities are seen. The whole thing is cheerfully coloured, and, whilst it is not claimed that it has any high aesthetic value, it is bright, it catches the eye, and it is pleasing and amusing to look at. No attempt has been made to divide the room into two compartments, since the lighting and the picture together succeed in creating the suggestion of a warm and friendly atmosphere.

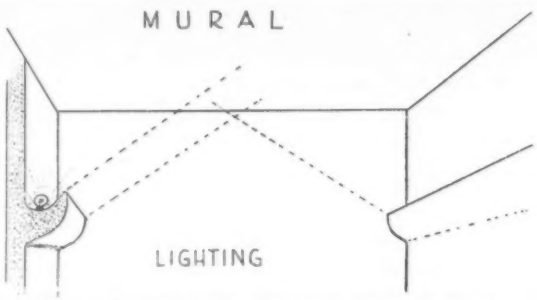

FIG. 1.—Diagram showing lighting of picture on ceiling.

Investigation and Questionary

One hundred patients, almost all of whom had received the same premedication, were closely observed as they came into the anaesthetic room and were assessed as being in one of three categories: awake, sleepy, or asleep. Attention was not drawn to the painting, but the patients were watched to see whether or no their attention was caught by it. Spontaneous comments were noted as being favourable, unfavourable, or not made. Apprehension was noted as being marked, moderate, or absent. The next day the patients were visited and the incidence of amnesia was estimated by asking if they remembered seeing the picture: their previous remarks were confirmed or altered and further comment was invited.

Results

Two notable features emerged from this survey. Firstly, the large majority of patients noticed the picture ;

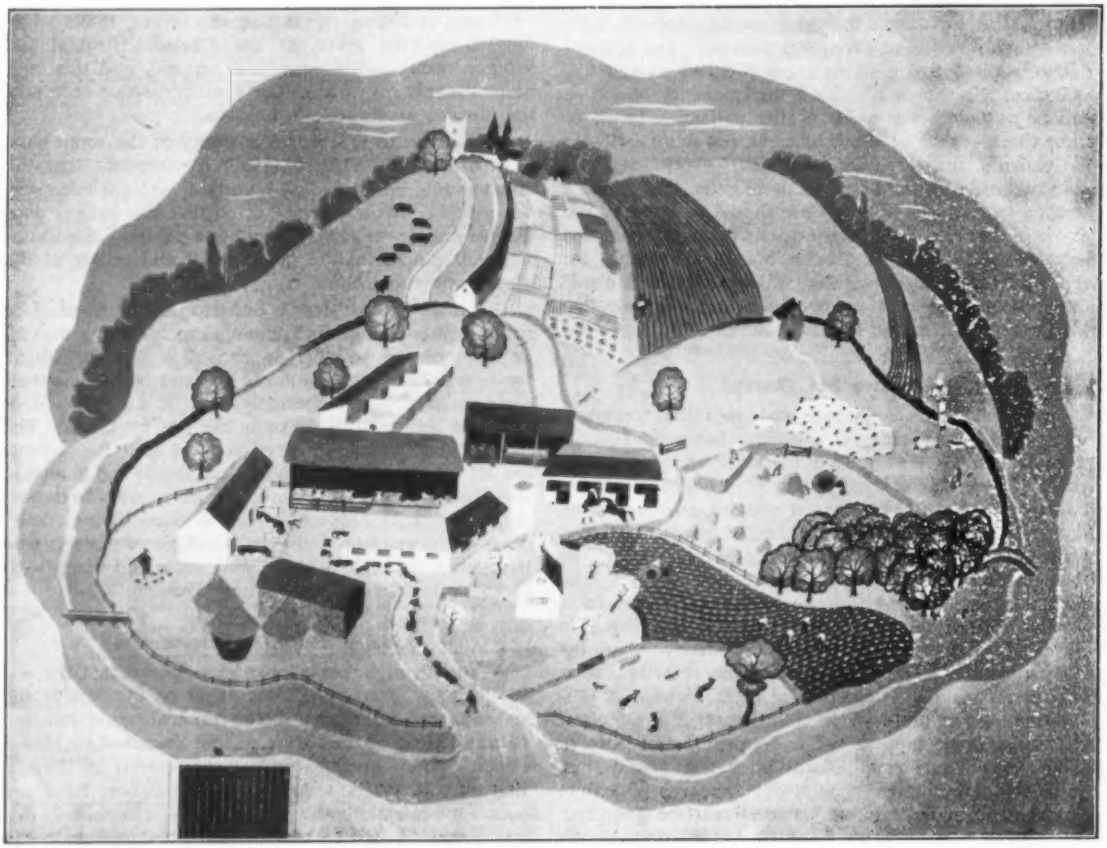

FIG. 2.—Photograph of painting.

and, secondly, they liked it and frequently were fully appreciative of its purpose, thus proving the value of such an idea (Fig. 3).

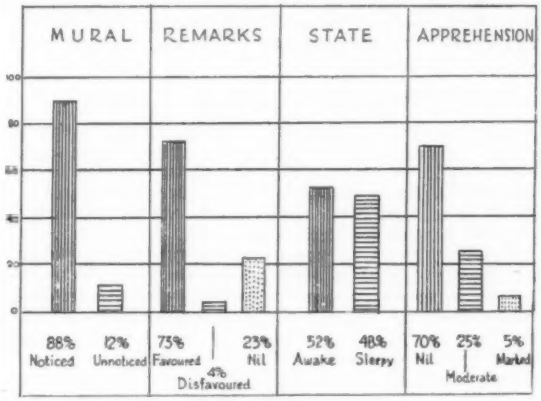

FIG. 3

Ninety-seven of the patients were premedicated with "omnopon," ¼ gr. (20 mg.), and scopolamine, 1/150 gr. (0.43 mg.): the other three had pethidine or morphine and atropine.

Fifty-two were marked as being fully awake on arrival at the room, 48 were sleepy, and none wholly asleep.

Apprehension was noted as absent in 70 instances, moderate in 25, and marked in 5 patients.

Of the 88 patients who had noticed the picture, 77 made spontaneous comment on it and 11 obviously focused their attention upon it. Twelve patients apparently did not notice it at all, though this estimate appears to be incorrect, since two patients put in this category later stated that they remembered having seen it.

It was soon realized that these latter groups of figures could not be claimed as representing a true picture of patients who, under the influence of narcotic drugs and without any prompting, would notice the picture. Though the patient's attention was deliberately not directed to it, it was found that they had generally been briefed in the ward beforehand by others who had already seen it. One patient raised quite vigorous objection to having her thiopentone in the corridor, on the grounds that she did not want to be done out of seeing the picture that she had heard so much about in the ward. While this unexpected development certainly detracts from the value of the observation as such, it provides ample proof of the appreciation by the patients.

Amnesia.—The degree of this, as estimated by questioning the patients next day, appears to be surprisingly small. In only four instances did those who had noticed it at the time have no recollection of it the next day. Again it is necessary to treat this figure with reserve, since talk in the ward may well have rekindled or reinforced the patient's memory.

Remarks and Comments made by Patients

The remarks made in the anaesthetic room were graded as: favourable 73, unfavourable 4, nil 23. Twenty-four hours later these were slightly modified to: favourable 81, unfavourable 2, nil 17.

Of the unfavourable remarks or comments, one patient said that she had been worried at the time and that the painting did nothing to divert her thoughts; another "just didn't like it"; a third thought the subject matter more suited to children, but later did not substantiate this.

The favourable comments which were made not only proved the justification of the idea but also threw an interesting sidelight on the patient's outlook. In the large majority the comments were of the well-known stock variety: "Ever so nice," "smashing," "terrific." Of those who expressed their opinions more clearly, the almost unanimous observation was that it was a helpful form of distraction: "Takes the mind off worry," "off the operation," "off things" "something to think about." The most interesting type of remark came from a handful of patients some of whom were actually questioned after this series had been completed. These remarked with quite sincere and ingenuous candour that what surprised them most was that the doctors should think sufficiently about the patients' feelings to consider doing such a thing for them. "I knew the doctors were nice, but I didn't know they thought that much about us." "Fancy the doctors thinking about us that much." "If you think enough about us to do that for us, this must be a good place." There was no sense of complaint in these remarks: they merely expressed genuine surprise, and, serving as a salutary fulfilment of Burns's desire that we might see ourselves as others see us, should make us wonder to what extent the unspoken suggestion of lack of humanity may be justified.

Discussion

The equipment of our hospitals daily becomes more involved and techniques more scientific, but these cannot be appreciated by the patient, and it would be a pity if such advances were accompanied by a loss of those human touches which are of such comfort to him. The mind of the person waiting in the anaesthetic room is particularly receptive to external impressions, whether unpleasant or agreeable—and the latter are correspondingly more particularly appreciated. Moreover, the patient who is in a state of considerable anxiety at this stage thereby constitutes a more serious risk. Any reasonable steps taken to minimize this are justified.

Summary

A description of the lighting and of the painted ceiling of the anaesthetic room at the Chelsea Hospital for Women is presented. The aims of such decorations are discussed. Observations on patients show that a large majority notice it and appreciate its purpose. It achieves its object of distracting the mind from worry; the financial expenditure is thus justifiable and commendable.

As in the case of the Bart's picture, the artist was Mrs. Pamela Johnstone. My grateful thanks are also due to the resident anaesthetists, Miss M. Simpson and Miss J. Casserley, for their considerable help in completing the questionary.

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TRENDS IN TUBERCULOSIS

SYMPOSIUM IN PHILADELPHIA

[FROM A SPECIAL CORRESPONDENT]

An international symposium on tuberculosis, held in Philadelphia from November 19 to 22 and sponsored by the Deborah Tuberculosis Sanatorium and Hospital, permitted specialists in research and practice to discuss current issues in a semi-informal manner not usually achieved at international conferences. Representatives from Britain, Canada, France, Norway, U.S.A., and W.H.O. were grouped into six panels before a medical audience of several hundred. Three panel sessions are reported here; the unreported panels were on the respective roles of home and hospital in the management of the tuberculous, case-finding, and the surgery of pulmonary tuberculosis.

"Primary Chemoprophylaxis"

Professor S. RAFFEL (San Francisco) introduced the subject of chemoprophylaxis with isoniazid in persons exposed to tuberculous infection. The panel—Professor W. MCDERMOTT (New York), Dr. G. CANETTI (Paris), Dr. J. HOLM (W.H.O.), Dr. EDITH M. LINCOLN (New York), Dr. L. H. SCHMIDT (Cincinnati), and Professor G. P. YOUMANS (Chicago) — agreed that this be termed "primary chemoprophylaxis" if tuberculous infection had not yet occurred, and "secondary chemoprophylaxis" if infection (with positive tuberculin reaction) had occurred but no disease was manifest. The trend of their opinion was that "primary chemoprophylaxis" in contacts might suppress an infection completely in some instances, or postpone multiplication of the bacilli—perhaps to a more favourable time—and that these gains might be particularly valuable in infants in a highly infective environment; a short course of isoniazid with break of contact might be a good method of application.

The counter-arguments that even under drug cover infection might occur, and surviving organisms multiply after cessation of administration and without adequately having stimulated acquired immunity, were considered insufficient to deprive this method of a place in prevention. Combination with vaccination, probably using isoniazid-resistant B.C.G., was also discussed. The generally favourable view of "primary chemoprophylaxis"—even though its use be admittedly very limited—came as a surprise to at least one European panel member: there was indeed some retreat at a later session from the position taken at this one, when it was suggested by a participant that primary chemoprophylaxis should be used only in cases of strong and continuing contact and in conjunction with vaccination; indeed, there was general agreement that this procedure needed further investigation before it would be possible to be dogmatic about its usefulness.

"Secondary Chemoprophylaxis"

The use of isoniazid in individuals already tuberculin-positive but without manifest disease — "secondary chemoprophylaxis" — was considered to be more often indicated, particularly in young children and adolescents, more especially if highly tuberculin-sensitive. Recent tuberculin-conversion was included under these indications. The likelihood of drug-resistant organisms emerging as a result of treating such latent infections was considered remote, because bacilli would probably be too few and too sluggish and cavitation was not to be expected. However, while the majority of the panel thought isoniazid relatively non-toxic and safe to use prophylactically over long periods, some quoted slight and subtle effects—for example, on intellectual efficiency—after prolonged administration in otherwise healthy persons.

There was intense discussion on whether drug administration in the presence of latent tuberculous infection might interfere with development of naturally acquired immunity, particularly if started soon after the occurrence of the infection. Opinions were divided, but the majority felt that there was not too much fear of this. No definite recommendations were given for the duration of "secondary chemoprophylaxis."

Relapse After End of Treatment

After considerable difficulty in agreeing whether relapse should be defined in terms of radiology or bacteriology, and whether its consideration should be confined to the period after discontinuation of chemotherapy, the panel—Dr. G. MIDDLEBROOK (Denver), Dr. J. D. STEELE (California), Dr. O. AUERBACH (New Jersey), Mr. F. R. EDWARDS (Liverpool), Dr. I. EPSTEIN (Brooklyn), Dr. S. FROMAN (California), Dr. J. W. RALEIGH (Washington), Professor J. M. ROBSON (London), and Dr. W. STEENKEN, jun. (Saranac Lake)—discussed behaviour of experimentally infected animals after the end of prolonged treatment with isoniazid alone or in combination with other drugs.

The situation then was a complex one, and non-specific host resistance and acquired specific immunity were important factors. Under some circumstances drug-sensitive organisms could still persist in a "sleeping state" without macroscopic relapse. Although cortisone had failed experimentally to stir persisters into activity, it had been found that, if this steroid was followed by isoniazid plus pyrazinamide during the treatment phase, their incidence was reduced; possibly the chance of relapse might also prove to be reduced. In man, post-treatment relapse was more often due to resistant than to sensitive organisms.

There was a tendency in this session to discuss relapse as it applied to the most favourable conditions of hospitalization and patient-control. The considerable difficulty in re-treatment created by relapse after inadequate initial treatment, and the extent of the public health risks of such patients who excrete drug-resistant organisms, often catalase-positive when the regime has included isoniazid, were not given much attention. An interesting and apparently new piece of incidental information from a participant was that the incidence of neuro-toxicity accompanying cycloserine administration had been found, like that from isoniazid, to be reduced if pyridoxine was given as well.

Control of Tuberculosis

This subject, introduced by Dr. J. HOLM, of W.H.O., was the only one to be given an international flavour; although enthusiasm, engendered by the immediate prospects in countries like U.S.A., got a little out of hand (so it seemed to this correspondent) when it was suggested later that W.H.O.'s immediate programme should include a world campaign for the eradication of the disease. However, the panel—Professor D. A. COOPER (Philadelphia), Dr. G. CANETTI (Paris), Dr. P. D'ARCY HART (London), Dr. J. E. PERKINS (New York), Dr. W. B. TUCKER (Washington), and Professor J. L. WILSON (Philadelphia)—agreed that for many countries the sights still needed to be lowered and the objectives much more modest. In such countries not only was the mass attack on the disease still at the planning stage but the risks of building up drug-resistant populations under the difficult conditions of treatment had not yet been defined. International tuberculosis statistics had become increasingly unsatisfactory since mortality figures had been slashed by drug therapy; morbidity, while useful nationally, was unsuitable for international comparisons. For the latter, random prevalence surveys (by *x*-rays, sputum examination, and tuberculin-testing), carried out in a standard manner as had been developed by W.H.O., could supply the necessary information.

The main specific attacks were by B.C.G. and chemotherapy, chemoprophylaxis being in its infancy. In W.H.O. there were no doubts about the efficacy of correctly

(Continued at foot of next page)

To-day's Drugs

With the help of expert contributors we publish below notes on a selection of drugs in current use.

Injection of oxytocin *B.P.*

Pitocin (Parke, Davis).

Syntocinon (Sandoz Products).

Injection of oxytocin *B.P.* and pitocin contain the oxytocic principle of the pituitary; syntocinon is synthetic oxytocin. Clinical trials have shown there are no qualitative or quantitative differences between the naturally occurring and the synthetic oxytocins. The indications and contra-indications are therefore the same for both. Oxytocin preparations may be given intramuscularly or by intravenous infusion. When used for the induction of labour or for the treatment of hypotonic uterine inertia, the more easily controlled continuous intravenous drip is preferable to intermittent intramuscular injections, but it should be restricted to hospital practice. For the prevention and treatment of post-partum haemorrhage, ergometrine is more widely used than oxytocin, but some prefer to supplement the former with the latter when bleeding is severe.

Preparations of natural oxytocin are all standardized to contain 10 units per ml. Syntocinon is also available in a strength of 1 unit per ml. This must be appreciated if confusion is to be avoided, but the weaker solution has a practical advantage, especially for intermittent intramuscular injections.

N.H.S. basic price: inj. oxytocin *B.P.* and pitocin, ½-ml. ampoules (5 units), 6 for 5s. 6d.; syntocinon, ½-ml. ampoules (5 units), 6 for 5s. 4d., and 2-ml. ampoules (2 units), 6 for 4s. Larger ampoules of all preparations are also available.

Price change.—Basic N.H.S. price of "cobalin" (Paines and Byrne), six 1-ml. ampoules 100 μg. ("To-day's Drugs," December 20, 1958, p. 1530), is now 2s. 6d.

Neomin tablets (Glaxo).—Each tablet contains 0.5 g. neomycin sulphate; the 350 mg. shown for this drug ("To-day's Drugs," December 27, 1958, p. 1591) is the equivalent amount of neomycin.

(*Continued from preceding page*)

applied vaccination, and the current M.R.C. trial (as well as the famous pioneer investigation associated with the name of Professor J. D. Aronson, who died in October) was cited. The panel seemed to accept this viewpoint in spite of the rather disturbing results obtained in the U.S. Public Health Service investigation. The fear of losing the value of the tuberculin test could be alleviated by not vaccinating generally before school age, though a non-sensitizing vaccine, should this become available, might be even better. However, the majority view of the American panel members was against mass vaccination of any groups in the present state of tuberculosis in their country—this being in contrast to Canada, where in some parts both infants and school-leavers are vaccinated. A plea for a national register of vaccinated individuals was made by one member.

The panel felt that, in order to detect cases for chemotherapy at an early stage, case-finding needed to be improved. Mass radiography is changing its character, and the success of intensive community surveys such as that recently made in Glasgow was mentioned. The recent tendency towards domiciliary treatment has focused attention on problems of self-administration of drugs in chronic diseases, and the panel urged more study on this subject of world importance.

Correspondence

Because of heavy pressure on our space, correspondents are asked to keep their letters short.

Haemorrhage and Fibrinogen Depletion

SIR,—Simplicity is often the keynote of success for investigations which may have to be undertaken in an emergency, and the modification of a well-accepted and widely practical technique described by Mr. G. L. Bourne and Mr. J. A. Riedel (*Journal*, December 13, p. 1454) is therefore to be commended. It is possible, however, that we have of late attached too much importance to the single factor of fibrinogen depletion in a syndrome where arrest of haemorrhage may be dependent on other defects in the clotting mechanism as well as factors associated with defective uterine action. In particular, we would like to emphasize the following points.

Post-partum haemorrhage frequently occurs in cases of accidental haemorrhage even when the fibrinogen level has been restored to normal. This could mean that other factors concerned with the clotting mechanism are deficient, and, if this is so, plasma may be more effective than fibrinogen in correcting the coagulation defect. Conversely, in many cases of accidental haemorrhage, post-partum haemorrhage does not occur even in the presence of proved fibrinogen depletion.[1] Similarly, patients with thrombocytopenic purpura do not have post-partum haemorrhages if uterine function is normal. This confirms the fact that arrest of uterine haemorrhage is primarily due to mechanical factors. Therefore, it may be asked whether in fact anything is to be gained by intensive correction of fibrinogen depletion, particularly when it is known that spontaneous rectification of the defect may occur. Further, it may be asked whether positive harm may result from administration of fibrinogen or plasma. It is commonly accepted that the primary factor responsible for the coagulation defect is liberation of thromboplastin from the damaged placenta. So long as this source of thromboplastin remains, transfusion with fibrinogen or plasma may encourage further intravascular deposition of fibrin and stimulate production of lysins.

Perhaps an even more important and little recognized risk is that of citrate intoxication. It has been shown by Ludbrook and Wynn[2] that dangerous blood-citrate levels may be reached by giving stored blood at a rate of one bottle in five minutes. The citrate content of triple-strength plasma is approximately three times that of stored blood, and therefore rapid administration of such a solution may be particularly dangerous.

The potential risk is illustrated by a recent case of hypofibrinogenaemia treated by rapid transfusion with double- and triple-strength plasma. Attempts were made to give the plasma rapidly, but on each occasion the patient complained of pain in the chest and generalized paraesthesiae. The symptoms were relieved by reducing the rate of transfusion. Subsequently she developed frank tetany, which was immediately relieved by intravenous administration of calcium gluconate. We wonder if a similar disturbance could have been responsible for the "rigors" described in the case of Messrs. Bourne and Riedel.

Resuscitation with intravenous fluids should be started as soon as possible, but plasma substitutes are

best avoided, as they may aggravate the coagulation defect.[3] As soon as resuscitative measures have been established, early evacuation of the uterus should be encouraged. Indeed, artificial rupture of the membranes should be performed at the earliest possible moment. Caesarean section would result in even more rapid removal of the uterine contents and would possibly be a preferable form of treatment if it could be shown that there was no serious risk of haemorrhage from the abdominal and uterine wounds. In the light of recent observations we suggest that, whilst the diagnosis and correction of fibrinogen depletion may be important in the management of accidental haemorrhage, this should not be unduly emphasized at the expense of other aspects of treatment. It is also worthy of consideration that our therapeutic methods may have harmful effects.—We are, etc.,

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Protein Anabolizers

SIR,—It was interesting to read the article by Dr. E. Woodford-Williams and Mr. D. Webster (*Journal*, December 13, p. 1447) reporting the fact that valuable protein anabolism was readily produced in four underweight old men by norethandrolone with a dose of 30–50 mg. daily. This paper would, however, have been more generally useful if the subjects chosen had been females.

Norethandrolone is no more anabolic than testosterone propionate, and, although this action of the latter has been known for the last 20 years, its use has been neglected for this purpose in males. Surely it is much more reasonable to give testosterone derivatives to old men (as long as the presence of prostatic carcinoma has been eliminated)? What would it matter, if, in fact, its androgenic effect were significant? It might even be a boost to their morale. How is it possible to state that no androgenic effects were observed after the use of norethandrolone in males, unless the subjects were eunuchoids?

I feel that such an article published in the *British Medical Journal*, which is widely read by some who are not fully aware of the anabolic actions of testosterone or methyltestosterone, may lead to the gross misuse of norethandrolone for adult males, and at an unnecessarily high cost to the National Health Service. A daily dose of 50 mg. of norethandrolone costs 10s. 6d., whereas 75 mg. of methyltestosterone or 20 mg. of fluoxymesterone, which will produce equivalent protein anabolism, cost approximately 2s. and 2s. 6d. respectively. The great value of the availability of these new steroids like norethandrolone is their therapeutic usefulness for women and prepubertal children of both sexes, where a virilizing action is to be deprecated. Although a dissociation of androgenic and anabolic effects in a ratio of 1:15 has been found in rats given norethandrolone, it can be stated quite definitely that no new anabolic steroid has as yet become available for clinical use which does not have some slight virilizing effect in women and children, if given for long enough in full anabolic doses.—I am, etc.,

Bristol. GEORGE FOSS.

Lumbar Puncture

SIR,—While agreeing with some of the views expressed in your leading article on this subject (*Journal*, December 20, 1958, p. 1520), I would like to make a few comments. Except in cases of infection, examination of the lumbar cerebrospinal fluid (C.S.F.) seldom leads by itself to a specific and accurate diagnosis any more than does examination of the urine in diseases of the renal tract. The precise diagnosis may in fact be delayed by lumbar puncture (see below), and, as you say, the patient's condition may be made worse and his life even endangered.

In earlier days lumbar puncture was used not only to examine the cytology, bacteriology, and chemistry of cerebrospinal fluid, but also to assess the presence of raised tension within the central nervous system and/or the possibility of block somewhere in the spinal canal. Nowadays raised tension is much more safely estimated by clinical, ophthalmoscopic, and radiological methods. Although papilloedema is fairly constantly associated with raised intracranial tension, sometimes a diminution of the calcium content in the dorsum sellae is an earlier sign. The demonstration of a block to the passage of C.S.F. by means of lumbar puncture gives no indication of the precise site or nature of the block and may lead to a deterioration in the patient's condition by further damaging the spinal cord as a result of suddenly altering the pressure. Thus, for example, *benign* spinal tumours such as a neurofibroma or meningioma may be suspected when certain signs of cord compression are present. A lumbar puncture will nearly always show an increase of protein in the C.S.F. and a partial or complete block. The exact level of the lesion is still not known, and meanwhile the removal of a few ml. of C.S.F. may so upset the intrathecal hydrodynamics that the cord becomes irrevocably compressed within the next few hours or days. This has happened.

My plea is that the examination of the lumbar C.S.F. should be made, in many cases, in conjunction with a more positive diagnostic procedure aimed at pin-pointing the lesion and perhaps leading to a firm opinion regarding the pathology at the same time.

Two general examples may be quoted, (*a*) where an intracranial mass and (*b*) a spinal mass is suspected. In the former case, your own example will serve. "It is generally safe to carry out the procedure (lumbar puncture) with caution in patients who are believed to have an infiltrating neoplasm in one or other cerebral hemisphere but who show no clinical evidence of increased intracranial pressure." In neurological work one meets many such cases. Whether the fluid is shown to be normal or to contain an excess of protein, one still cannot be certain that (*a*) a tumour is present, (*b*) if present that it is infiltrating, or (*c*) if it is intracerebral or extracerebral (e.g., meningioma), or (*d*) if cerebral atrophy is the correct diagnosis. If a controlled fractional air encephalogram is carried out simultaneously, many of these doubts can be resolved and a specimen of fluid collected at the same time.

If a spinal mass is suspected, a positive contrast substance should be introduced (about 3–5 ml.) and an equivalent amount of C.S.F. removed at the same time. The information obtained from the combination of a myelogram and C.S.F. examination, preceded by plain *x*-rays, is often sufficient when added to the history and physical examination to allow a precise diagnosis to be made.

In your leading article you draw attention to leaking C.S.F. after lumbar puncture. I agree that this is undesirable, but for an additional reason. In my experience the important leak is into the subdural space, not the extradural space, as you suggested. Even with the most careful technique it is often impossible to prevent C.S.F. from seeping into the potential

subdural space and thus converting it into an actual space at the expense of the subarachnoid space. Such a state of affairs usually precludes a lumbar subarachnoid puncture for ten or more days. Thus, if it is desired to perform a myelogram or an air encephalogram shortly after a lumbar puncture, the examination will often prove fruitless. The C.S.F. may be easily tapped, but if the contrast substance, be it air or "myodil" (ethyl iodophenylundecanoate), is injected a satisfactory examination cannot be made, as only the subdural space will be outlined. It might be supposed that a cisternal injection would overcome the difficulty, but this is by no means certain, as the C.S.F. can strip up the subdural space all the way to the foramen magnum and above.

To summarize: if a space-occupying lesion is suspected, either within the cranium or spinal canal, it is often wiser to undertake the double investigation of introducing the appropriate contrast substance and collecting the C.S.F. specimen simultaneously.—I am, etc.,

London, W.1. J. W. D. BULL.

SIR,—Descriptions of the technique of lumbar puncture usually omit two helpful points which are not widely known amongst housemen on whom the responsibility for lumbar puncture often rests: (1) When the obese patient lies on his side with the knees "up to his chin," the spine is rotated so that the point of the needle should be raised about 5 degrees at least from the horizontal. (2) The conscious patient can identify accurately the position of the needle point in relation to the mid-line.

As you point out in your leading article (*Journal*, December 20, p. 1520), it is not necessary—one might say not desirable—to infiltrate deeply with local analgesic. If the patient feels pain when the needle is inserted he should be asked to state which side of the body, right or left. If he says definitely one or the other the needle should be withdrawn to the subcutaneous tissues and the direction altered accordingly. If the needle is in the mid-line the puncture is, as you state, virtually painless.—I am, etc.,

Birmingham, 15 W. M. PHILIP.

SIR,—Your leader writer (*Journal*, December 20, p. 1520) commends the widely held view that headache coming on after lumbar puncture is the result of continued oozing of cerebrospinal fluid through the puncture hole. This theory takes no account of the fact that symptoms do not arise after accidental lumbar puncture by the caudal route, as long as only a few drops are allowed to escape.[1]

In the practice of orthopaedic medicine, it often happens that epidural local anaesthesia is required for diagnostic or therapeutic purposes. Once in each few hundred inductions, a patient is encountered whose dura mater ends abnormally far down and the needle introduced intrasacrally via the hiatus pierces the theca. Cerebrospinal fluid drips out as soon as the stylet is withdrawn. Nothing is injected, of course, and the needle is taken out at once. The patient, who lies prone during the insertion of the needle, can get up and walk home without further ado. As long as no more than a couple of drops are allowed to emerge, he has no symptoms afterwards. Yet a puncture at the lowest point of the dura mater is ideally situated at the point of highest pressure—moreover, inferiorly instead of posteriorly—and leakage must take place as soon as the patient stands up. The fact that no precautions are necessary to avoid headache after this sort of unintentional lumbar puncture appears related to the tiny amount of fluid that escapes. There is none of the sudden lowering of pressure that occurs with removal of enough fluid to serve diagnostic purposes. This seems the important factor, and subsequent seepage immaterial.—I am, etc.,

London, W.1. JAMES CYRIAX.

REFERENCE

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Artificial Insemination

SIR,—My letter in your last issue (*Journal*, December 27, p. 1595), in which I sought the assistance of family doctors in obtaining evidence on this matter, contained a serious inaccuracy. I stated that the Council of the Association had decided to submit evidence to the Departmental Committee; in fact, Council has specifically deferred any decision on this point—until the possible nature of such evidence is in its possession.

I greatly regret that this misrepresentation of the position appeared in my letter, and hope that its readers also read—in the same issue—the report of Council's debate on the subject (*Supplement*, December 27, p. 270), which made the inaccuracy apparent.—I am, etc.,

B.M.A. House, Tavistock Square, London, W.C.1. J. R. NICHOLSON-LAILEY, Chairman of the Science Committee of the B.M.A.

Aspirin and Intestinal Haemorrhage

SIR,—Individual sensitivity to aspirin which may lead to very serious complications should be mentioned in connexion with the interesting article by Dr. L. Th. F. L. Stubbé (*Journal*, November 1, p. 1062).

One of the patients, a 55-year-old lawyer, whom I saw in neurological consultation because of acute cervical disk syndrome with painful irritation of the C7 root, had been taking tablets containing aspirin, phenacetin, caffeine, and codeine four-hourly for four days after admission to hospital. When I saw him he was pale, anxious, and restless, and in addition to his pain complained of two recent spells of extreme weakness with cold perspiration and severe anxiety. On further questioning, the patient admitted having tarry stools for a couple of days. His R.B.C. count was 3,540,000. Hb 7.2 g. (46%). He was given two blood transfusions and all medications were stopped, with satisfactory improvement. On the *x*-ray of the gastro-intestinal tract there was only slight suspicion of a duodenal ulcer. However, as the patient recalled, for at least ten years before this last illness he was passing black stools whenever he took aspirin for any aches or pains. He gave no history of peptic ulcer during that period.

I hope that the above case will suggest more cautious use of this apparently quite safe remedy.—I am, etc.,

Ottawa, Canada. VICTOR SZYRYNSKI.

Leucotomy

SIR,—After reading the report of the discussion at the Royal Society of Medicine on the results of leucotomy (*Journal*, December 13, p. 1470), I found an omission which I think is of the utmost importance in the selection of cases for cortical undercut or any other type of surgery for depression and tension states. I have in

mind the age group. From my cases which were operated on by Mr. Geoffrey Knight, it is clear that the best results were obtained amongst the middle age-group (45–60), where no prolonged hypertension was in existence. I fully support Mr. Knight's view that there are cases where we should not wait too long before resorting to psychosurgery.

I am also in agreement with Dr. Alick Elithorn's observations that there are at least two distinct groups of depressive states as opposed to Garmany's thesis of one group labelled "reactive." I think that there should never be any difficulty in arriving at the correct diagnosis if we carefully take the history of the case.—I am, etc.,

Mabledon Hospital, Dartford. G. BRAM.

Tuberculosis in Domestic Animals

SIR,—In his paper on the public health aspect of tuberculosis in domestic animals (*Journal*, November 8, p. 1133) Dr. M. A. Soltys expresses the view that avian tubercle bacilli are rarely found in cattle. As far as England and Wales are concerned, of the last 3,934 specimens from cattle examined for tuberculosis in this laboratory in connexion with the Attested Herds Scheme, 52 (1.3%) were found to contain avian type tubercle bacilli. Eighteen of these animals had progressive disease, including ten which had lesions in the udder with excretion of avian-type organisms in the milk. Specimens from 870 (22%) of the 3,934 cattle contained tubercle bacilli of the bovine type, and human type was recovered from another seven.

With reference to tuberculosis in pigs, Dr. Soltys states that the bovine type is most common. While this was no doubt true in the past, and the bovine type certainly causes a more progressive disease in pigs, there is evidence that, with the rapid eradication of tuberculosis in cattle in this country, most tuberculosis in pigs to-day is caused by the avian type. Recently, tuberculosis has been confirmed at this laboratory in material from 64 pigs from different areas of England and Wales, in which lesions were detected at slaughter-houses; avian type tubercle bacilli were isolated from 44 (69%) and bovine type from the other 20.—I am, etc.,

Central Veterinary Laboratory, Ministry of Agriculture, Fisheries, and Food. IAN W. LESSLIE.

Antibiotics in Acute Tonsillitis and Otitis Media

SIR,—The letter in your issue of December 20 (p. 1530) from Dr. David Wheatley is interesting, but surely it presents only part of the picture. It is true that antibiotics may cut short an attack of tonsillitis, but what else do they do? The normal intestinal flora may be seriously affected, with repercussions on digestion and absorption from the gut. Attacks of tonsillitis are often recurrent. Antibiotic sensitivity and resistant strains of bacteria are an increasing menace. Perhaps the administration of antibiotics in the present open-handed manner may, in an appreciable number of cases, represent local victory but ultimate defeat.

I do most heartily agree that, if antibiotics are given, dosage must be adequate. Hit to kill. In the military field Montgomery has recently emphasized the point.—I am, etc.,

Farnham Royal, Bucks. M. E. M. HERFORD.

Early Diagnosis of Mental Defect

SIR,—I was glad to read Professor R. S. Illingworth's letter (*Journal*, November 29, p. 1355) and to note that we are agreed on the practical issues arising from early decisions about mental defect—in particular, that it is best to wait until at least five years before deciding on educability. The field of disagreement, if any, is narrowed to the question of whether we can recognize less severe forms of mental defect even, as Professor Illingworth says, "in the first two years and in many cases long before the first birthday."

The question turns partly on what we mean by severe. If the child is going to be an idiot (a severe case) then certainly the defect is often so gross as to be apparent early. In imbecility (medium range of mental defect) the position is much less clear. As to the mild cases, these are now regarded as educationally subnormal and are no longer classed as mentally defective for formal purposes. The question also hinges on why we want to know if the child is defective. For academic purposes a prediction which is right in 70% of cases may be quite useful, but it could not serve as a basis for a definite statement to the parents or any administrative action. It is a matter of general agreement among psychologists that the predictive value of tests in young children is low. My quotation was from Vernon.[1] Jones[2] ably sums up the results of longitudinal studies, and the following table (adapted) illustrates the poor correlation with tests done on infants.

Retest Correlations at 3-year Intervals

Ages in years	Ebert and Simmons[3] r	Honzik *et al.*[4] r
2 and 5	—	0.32
3 and 6	0.56	0.57
4 and 7	0.55	0.59
5 and 8	0.70	0.70
7 and 10	0.76	0.78
9 and 12 or 13	—	0.85

My own experience with infants who appear to be of imbecile level is that marked changes occur sufficiently often to make confident prediction unwise. I will therefore look forward with great interest to the publication of Professor Illingworth's survey in which he is able to demonstrate good prediction even with very young infants.—I am, etc.,

Fountain Hospital, London, S.W.17. BRIAN H. KIRMAN.

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Drug Treatment of Insomnia

SIR,—Dr. A. H. Douthwaite in his review of hypnotics (*Journal*, November 29, p. 1347) mentions in regard to the non-barbiturate methyprylone that clinical experience in this country is limited and that no side-effects have been reported. Methyprylone and glutethimide, another non-barbiturate drug, have been used by us as standard hypnotics in several hundreds of mental hospital patients, after controlled trials in 1955 had shown their superiority over placebos. Favourable results in controlled trials of methyprylone were also

published in your columns by Stewart[1] and by Thomson,[2] and of glutethimide by Rushbrooke *et al.*[3] Both drugs were found to be reliable hypnotics with no side-effects in ordinary dosage. However, there was one case of habituation to methyprylone and (at least) two cases of habituation to glutethimide, with features such as confusion, slight ataxia, and slurring of speech. No reports on habit formation with these two (fairly recent) drugs seem so far to have been published. Several cases of habituation to the non-barbiturate methylpentynol were seen by us in the past,[4] and cases of addiction to ethinamate, another non-barbiturate hypnotic, have been reported in the German literature.[5 6] The case of methyprylone habituation occurred in a young female alcoholic: she took the drug habitually in increasing doses after she had spontaneously recovered from a suicidal attempt in which she had ingested 25 to 30 (200 mg.) tablets of methyprylone. Recovery without special measures being taken also took place in another alcoholic woman who bought 50 (250 mg.) glutethimide tablets from a chemist, took five tablets "just for the experience," and shortly afterwards —without remembering it—apparently another 12 tablets. However, the literature contains reports of successful suicide attempts with each of the four non-barbiturate drugs referred to. Thus whilst on the whole the non-barbiturate hypnotics in our experience seem safer than the barbiturates, especially for unstable personalities such as many alcoholics, with their frequent suicidal attempts[7] and their tendency to drug habituation, these new drugs are obviously not completely free from the risks of accidental, habitual, or deliberate overdosage.—I am, etc.,

St. Bernard's Hospital, Southall, Middlesex. M. M. GLATT.

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Hula-hoop Syndrome

SIR,—Recent correspondence (*Journal*, December 20, p. 1531) should not be allowed to discourage the use of the hula-hoop as a means of exercise and pleasure. It is obviously bad for it to be practised for several thousands of revolutions at a time, particularly since habitually it is done only in one direction. Observation shows that a person who habitually tends to stand on the right leg will perform the action in a clockwise direction, while the left-leg-stander will reverse this procedure. Safety lies in insisting on the child being able to perform the exercises equally in both directions.—I am, etc.,

London, W.1. GUY BEAUCHAMP.

Iron in the Home

SIR,—Under Medical News (*Journal*, December 13, p. 1483), you draw attention to the importance of iron as a cause of poisoning in young children. When I read this I consulted three fairly recent textbooks of medicine and two standard first-aid books, the latter intended for Red Cross and St. John Ambulance use. None of these referred to any specific treatment for iron poisoning. It appears to me that this is a serious omission, and that an equally serious one is the failure of the manufacturers of iron preparations which can be bought over the counter to indicate on their containers the symptoms, dangers, and treatment of iron poisoning.—I am, etc.,

Dublin. JOHN FLEETWOOD.

Buzzers for Bed-wetters

SIR,—Referring to the article "Treatment of Nocturnal Enuresis by the Electric Alarm" by Drs. T. H. Gillison and J. L. Skinner (*Journal*, November 22, p. 1269), and the numerous inquiries received as a result of the letter from Dr. Margaret White (*Journal*, November 8, p. 1165), the following information may be of interest:

Enuresis clinics in Croydon form part of the School Health Service. Machines are bought from the Orphan Homes of Scotland, Bridge of Weir, Renfrewshire, and loaned as items covered by the loan of home-nursing equipment under Section 28 of the National Health Service Act. The Ministry of Health have agreed that this is permissible.—I am, etc.,

Public Health Department, Croydon. S. L. WRIGHT.

Psychotherapy in General Practice

SIR,—Emphasis has been given in your columns recently to the role of the general practitioner as a clerk who merely directs patients to hospital for treatment. This is certainly true in the field of psychological medicine. However, many of us must well remember the psychiatric out-patients of our student days, where the usual therapy was in tablet form, with some smooth words of reassurance. Little else can be expected, in view of the long waiting-lists and the small amount of time available for each patient. Surely it is here that the general practitioner could come into his own. Knowing the family, the background, and the home of his patient, he is in the key position to give psychotherapy. The only requirements are training and time.

I should like to suggest that a course in psychotherapy be established for general practitioners, with a diploma upon completion. The general practitioner should receive a fee for his therapy outside the normal remuneration, as with eye-testing and obstetrics. The possession of a diploma as envisaged could put one on the "Psychotherapeutic List." I should like to see this as a specialist service of the general practitioner with a corresponding reward. In the above context my definition of psychotherapy would be sessions of counselling, in which one of the most important factors is the confidence established by the doctor. Benefit could be given to patients suffering from conditions such as asthma, allergies, peptic ulcerations, dermatitis, migraine, and ulcerative colitis by a deeper understanding of their problems.—I am, etc.,

London, S.E.10 C. A. FOX.

Case for Diagnosis

SIR,—I wonder how many cases diagnosed in general practice at this time of the year as influenza are in reality mild forms of infective hepatitis?

A patient of mine, a man aged 36, called me to see him on November 26. He complained of general malaise, headache, anorexia, and vomiting. On examination there was a pyrexia of 103° F. (39.4° C.), pulse rate 120, but no

other physical signs. On November 28 I visited him again. His wife told me he had been semi-delirious at night and still afflicted with extreme nausea and headache, temperature 102° F. (38.9° C.), pulse 120. His urine was dark-coloured. On shaking the urine in a test-tube there was at least 2 in. (5 cm.) of froth on 2 in. of urine. The froth had the faintest yellow tinge, and only partially settled after standing for five minutes. On December 1 his condition had improved. Pulse and temperature were normal. Urine remained as before with persistent white froth. At no time was the patient tender on palpation in the right hypochondrium. He has continued to improve. There has been no clinical jaundice throughout. On December 4 there was still 1 in. (2.5 cm.) of froth on 2 in. of urine, the froth being quite colourless.

It would be interesting to hear whether other practitioners have seen cases of this kind, which I conclude was one of infective hepatitis without jaundice, the frothiness of the urine being due to the excretion of bile salts. The "froth test" can be applied in any clean empty medicine bottle, and might help to sort out at least some of the cases of P.U.O. we meet in general practice. When positive it gives also a useful indication of the progress of the disease, becoming noticeably less marked as the patient's clinical condition improves.—I am, etc.,

Huddersfield. S. L. HENDERSON SMITH.

Bronchograms for Asthmatics

SIR,—Dr. Forde Cayley's letter expressing his anxiety in doing bronchograms on asthmatic subjects (*Journal*, November 22, p. 1292) deserves some sympathy. Quite apart from the effects of hydrocortisone in such cases, it still does not appear to be generally appreciated that laryngeal and endotracheal local anaesthesia is quite superfluous in bronchography, provided an oily contrast medium such as propyliodone 60% is used and the crico-thyroid puncture method is employed. Patients who have undergone both the oral and crico-thyroid puncture methods always express preference for the latter.—I am, etc.,

Ormskirk County Hospital, Lancs. K. D. FORGAN MORLE.

Too Many Tonsillectomies ?

SIR,—Dr. I. M. Librach (*Journal*, October 18, p. 976), referring to tonsillectomy, asks: "Why operate at all in the average case ?" I dislike the term "average," but, as 20% of schoolchildren in this country undergo the operation, the question is still a good one. Dr. Librach goes on to exhort E.N.T. surgeons to examine conscientiously and scientifically their indications for operation and follow-up results. The answer is not so simple as this. The James Mackenzie Lecture on "The Art of Consultation" (*Journal*, November 29, p. 1349) deserves to be widely read. In this admirable address Dr. G. F. Abercrombie referred to the general practitioner as the captain of the team. This is particularly so in the case of childhood ailments for which removal of tonsils and adenoids is so frequently advised. The E.N.T. surgeon must obviously be responsible for the final decision to recommend operation; for the most part, however, he is entirely dependent on the presentation of the case by the family doctor.

I believe that E.N.T. surgeons to-day are increasingly conservative, and are well aware that, while in certain cases tonsillectomy remains a valuable procedure, it is no panacea in childhood. A major reduction in the frequency of this operation will take place when more general practitioners feel, as many already do, that with patience and reassurance surgery may be avoided.—I am, etc.,

Hull. J. S. MARTIN.

Malignant Melanoma

SIR,—A housewife, aged 33, was recently admitted to hospital, where a diagnosis of irreducible femoral hernia was made. At operation the lump in the groin was found to be extraperitoneal fatty tissue infiltrated by hard black nodules. Biopsy confirmed that these nodules were in fact secondaries from a malignant melanoma. Post-operatively it was discovered that a mole, which developed in a week at the site of a hypodermic injection, had been removed from the patient's thigh four years previously.

I feel it is a remarkable coincidence that the site of a needle puncture and a newly developed melanoma should be identical. Could it be that trauma can initiate the development of a malignant melanoma where there was no previous benign lesion ?—I am, etc.,

London, N.W.10. E. LARKIN, Medical Student.

Appendicectomy in the Obese

SIR,—It is usually the task of junior resident surgeons to operate on cases of acute appendicitis, and these operations, though frequently easy, may be exceedingly difficult. This is particularly so in obese people, especially those with protuberant or pendulous abdomens, when even the anterior superior iliac spine may be impalpable beneath a mound of fat.

In these circumstances one is inclined not to operate but to treat them conservatively, hoping that the acute phase will subside and the patients will be induced to reduce their weight prior to an interval appendicetomy. But this is likely to prove dangerous, for I have found that there is little attempt to localize the infection. The immense fibro-fatty omentum present in these cases seems quite incapable of adhering to an inflamed viscus and walling it off from the general peritoneal cavity, with the result that the appendix often perforates, leading to a general peritonitis.

I have operated on a number of these unfortunate people, weighing 17–20 stones (108–127 kg.), and had always found it difficult until recently. In the usual supine position the incision made into the protuberant abdomen is on the side of a steep slope and the appendix is lying beneath coils of intestine and pounds of omentum. However, by tilting the patient to the left to an angle of about 45° by means of sandbags, one finds that the fat of the abdominal wall falls away to the left and an incision, preferably a transverse one in the skin starting from the anterior superior iliac spine, can be made in a horizontal instead of a vertical plane. On opening the peritoneum it is found that the abdominal contents have also fallen away to the opposite side, and the appendix is found lying on top and can be removed easily, little or no retraction being necessary. This is true whether the appendix is retrocaecal or not. May I commend this simple manœuvre to any of those resident surgical officers who are faced with a similar problem ?—I am, etc.,

St. Alfege's Hospital, London, S.E.10. R. F. BOLAM.

"Spit in Your Eye?"

SIR,—The following is culled from a medical registrar's report: "Fundi—the disk edges were blurred, there was marked arteriovenous 'nipping,' and there were scattered old and fresh haemoptyses throughout both fundi."—I am, etc.,

London, S.W.1. A. GILBY.

Charges of Indecency

SIR,—Mr. C. P. Harvey, Q.C., says that one can be charged with indecency by walking through a London park at night (*Journal*, November 22, p. 1257), and I can quite believe it. One can be charged if one uses, just as innocently, a public lavatory.

A few years ago I gave evidence for an Italian film director who was staying at a London hotel. He knew little English but had been told that there was a place called Soho where Italians lived, and, feeling lonely, he set out to find it. The evening was a cold one, and he visited on his way a public lavatory to pass urine. His search was not immediately rewarded, and, knowing no other lavatory, he returned to the same one again. In all he went to the same lavatory four times in an hour. He was arrested and charged with, I think, loitering with intent. No doubt all this sounds very suspicious unless one knows the sequel.

A careful physical examination showed that he had an enlarged prostate and his urine was full of sugar. Moreover, he was able to produce blood-sugar findings for the past four or five years which showed that he was a chronic diabetic. Sir Laurence Dunne, the magistrate, heard the evidence and dismissed the case, stating that the police had made a mistake.

This no doubt suggests a happy ending, but the poor fellow had had to spend a large sum of money in staying to combat the case and in professional assistance. Not a penny of this was refunded for what was an absolutely unfounded accusation.—I am, etc.,

London, W.1. CLIFFORD ALLEN.

Iatrogenesis

SIR,—I was intrigued, excited, and dismayed to learn from your annotation (*Journal*, December 20, 1958, p. 1521) that oxygen is "a potentially iatrogenic agent." Pausing only to consult my "Liddell and Scott," I rushed to the neonatal ward, but was disappointed to find that no physician had been produced in our incubators. Could you please tell me the optimum conditions for iatrogenesis? Producing a physician from a hat would enliven our Christmas party immensely.—I am, etc.,

Newport, Mon. PETER BIRKETT.

POINTS FROM LETTERS

Congenital Deaf-mutism

Dr. L. FISCH (Harrow, Middlesex), writes: Dr. John McKenzie (*Journal*, November 1, p. 1102) assumes that normal radiological appearances of the cochlea exclude an abnormality of the inner ear structures. I must confess my ignorance of the possibilities of radiological diagnosis of lesions of the organ of Corti. But I can give an example from one of my cases. In front of me I have a large series of *x*-rays of a temporal bone which was examined after it was taken from a profoundly deaf subject who died. A very careful radiological examination was carried out by an expert in radiology of temporal bones. The bony labyrinth was normal. I also have a histological picture of the same specimen. It shows that the organ of Corti is absent. Normal radiological appearances can and do exist in many congenitally deaf subjects whose hearing impairment is caused by a lesion in the nervous mechanism of hearing.

Obituary

E. S. CURTISS, M.B., B.S., F.F.A. R.C.S.

Dr. E. S. Curtiss, consulting anaesthetist to the King Edward VII Memorial Hospital, Ealing, and other hospitals in and near London, died on December 11.

Edgar Stuart Curtiss was born in 1905 and educated at St. Paul's School and St. Bartholomew's Hospital. Qualifying in 1926, he graduated M.B., B.S. in 1927 and held house appointments at Bart's and at the Metropolitan Hospital. He then went into general practice in Ealing, taking a special interest in anaesthetics. In due course he was appointed anaesthetist to the King Edward VII Memorial Hospital and to the Acton Hospital. Volunteering for service at the outbreak of the second world war, he served in the R.A.M.C. first as a general duty officer and later as an anaesthetic specialist, with the rank of major, in England, North Africa, and Italy. In 1944 he published a paper describing his experience with thiopentone sodium in N. Africa, based on 2,500 administrations. At the end of the war he returned to his practice in Ealing, but soon gave this up to devote himself entirely to anaesthetics. He obtained the D.A. in 1945 and was elected F.F.A. R.C.S. nine years later. He was awarded the Territorial Decoration in 1955.

Mr. J. W. S. LINDAHL writes: Stuart Curtiss was a first-class anaesthetist, not only in the technicalities of his specialty but also in the care and interest he took in his patients before and after operation. He also made some original contributions to the literature, notably a carefully worked out simplification of the postural method of local analgesia for intranasal operations. Outside his professional work he had wide interests, which included music, amateur dramatics, and railways. He spent many a happy day by himself at Swindon or Bristol, being especially fond of the engines of the old Great Western Railway. A keen golfer, he particularly enjoyed playing in West Sussex, a part of the country to which he was deeply attached. On his release from the Army he found himself still interested in Army matters and joined the Territorial Army, in which he was still serving at the time of his death. He had a strong sense of duty, and many a patient has reason to be grateful to him for his attendance at an operation because he felt that it would not be right to leave a difficult anaesthetic to a junior. A man of strong and definite opinions in many matters, he combined this with a great personal charm and an outstanding capacity for friendship, and there are many who are now remembering with gratitude his friendship and unobtrusive helpfulness. Stuart Curtiss had a very wide circle of real friends, and nobody could have deserved them more than he did. Our sympathy goes to his wife and two daughters, whose tireless support meant so much to him in his illness.

Sir JOHN NICHOLSON, Bt., writes: As the senior surviving officer of the old 95th General Hospital, which was among the earliest hospital units to arrive in Algeria with the First Army in 1942, I should like to pay my tribute to the part played by our anaesthetic specialist, Dr. E. S. Curtiss. Stuart Curtiss was an excellent anaesthetist, and, like all good modern anaesthetists, he played an active and effective part in the pre- and post-operative care of his patients. From my recollections, during the first year in which this hospital was functioning, some 4,000 operations (some of which were of a most hazardous nature) were carried through without a single death during operation, a clear enough tribute to Curtiss's professional skill. As an officer he also played a valuable part, particularly in improving relations between the various factions which from time to time made up this large and cosmopolitan unit; these comprised not only his brother officers and men, and the nursing sisters, but also various teams of attached specialists engaged in

research of one kind or another, the earliest teams of American surgeons and anaesthetists, who were attached to us in order to find out what it was all about, and visiting V.I.P.s of every description. When attempting to enlist my support for some liberal measure of reform in the somewhat austere conditions prevailing in the unit in the early days, Curtiss was apt to preface his remarks with, "I know I'm a bad type, but . . ." As a matter of fact this self-portrait was a most inappropriate one unless such qualities as loyalty, conscientious hard work, and complete integrity are characteristics which qualify for the description. His brother officers and colleagues of those difficult times will grieve to hear of his passing at a comparatively early age.

Dr. M. W. LLOYD OWEN writes: I should like to pay tribute to the late Major E. S. Curtiss on behalf of all members of the 17th (London) General Hospital, T.A., where he had been a member since 1950. From the very start it was obvious that he was going to be a tremendous asset to the unit, and with his happy knack of making friends quickly and easily he soon became one of our most popular members. He carried out the tasks allotted to him with skill and efficiency, being a most excellent administrator. His charm, tact, and sense of humour were characteristics which contributed greatly to the smooth and happy atmosphere in the mess. People turned readily to him when in trouble, and the advice he gave was always sound and to the point. He enjoyed life to the full, and it was difficult to be in his presence for long without being infected with his spontaneous gaiety. The fortitude and quiet dignity with which he faced his inevitable end have been an example and inspiration to us all. The unit has lost a most loyal and lovable character.

SIDNEY WRAY, L.M.S.S.A.

Dr. Sidney Wray, who had been in practice at Ingham, Lincoln, for some 30 years, died at Ingham on November 8. He was 57.

The sudden and tragic death of Sidney Wray was not only a great shock to his many friends in Lincolnshire but a serious loss to the profession and the National Health Service in the area. He studied medicine at Manchester University, qualifying in 1927. He came to Ingham 30 years ago; he remained there for the rest of his life, running his scattered county practice with a conscientious attention to detail that was a model for others to follow. At any medical meeting Dr. Wray could be relied upon to supply his own detailed and accurate statistics of country practice in Lincolnshire. He was for many years a member of the Lindsey Local Panel Committee and was an original member of the Lincolnshire (Lindsey) Executive Council, local medical committee, and Lincoln No. 1 Hospital Management Committee, serving on this last body until his death. A representative in the A.R.M. for the Lincoln Division of the B.M.A. from 1942 to 1947, he served on the Rural Practitioners Subcommittee from 1942 to 1949. From 1948 to 1956 he was chairman of the local medical committee.

Dr. Wray made the study of law a hobby second only to his devotion to his medical work. This was a great help in his medical services committee work, and those who served with him on the executive council and its subcommittee will always remember his calm intervention when tempers were heated: "You must look at this in equity." Those who had the privilege of hearing some years ago his presidential address to the Lincoln Medical Society, when he spoke for an hour and a quarter without notes on "Negligence" and held his audience spellbound, will know that the legal profession sustained a loss when he decided that medicine was his career.

In the passing of Sidney Wray his patients have lost a physician and counsellor of the old school of general practice; his colleagues in the profession, not only in Lincolnshire, but throughout the East Midlands and in London, have lost a kindly friend and a great personality who did not spare himself in the service of others.—A. M. M.

A. C. T. and J. R. B. write: There will be many in the neighbourhood of Lincoln, and particularly in the villages around Ingham, who will be very grieved by the sudden death of Dr. Sidney Wray. As fellow practitioners who knew him well, we would like to pay tribute to him. He was a man for whom the practice of the art and science of medicine was life itself. He devoted himself for over 30 years to the people who sought his help over a wide area. Thoughtful and careful, he brought insight, understanding, coolness in emergency, and skill in diagnosis and treatment into every kind of home. His wide experience of all kinds of illness, in surgery, in midwifery, and in medicine, and in the ordinary and extraordinary problems of family life made him a trusted and well-loved family doctor. In another sphere, that of administration, Dr. Wray brought to his committee work a deep awareness of social history, a useful acquaintance with law, a vision of the possibilities of the future for a full health service, and a sense of humour which is so invaluable when opinions differ. He made a great contribution to the work of establishing the National Health Service in Lindsey and Lincoln City. His colleagues on the Lincoln Hospitals Management Committee, the Lindsey Executive Council, the local medical committee, and the Lincoln Medical Society will greatly miss his advice and genial company. He had forewarning of his last illness several years ago, and faced the future with a calm knowledge born of a serene mind. It is sad that he lived so short a time in the new home which he had prepared against the retirement which could not have been long delayed. To his wife and his daughters, and indeed to all to whom Dr. Sidney Wray meant so much, we offer our deepest sympathy.

C. M. BURRELL, B.M., B.Ch.

Dr. C. M. Burrell, general practitioner and surgeon in Cardiganshire, died suddenly at Aberystwyth on December 7. He was 70 years of age.

Charles Milwyn Burrell was the eldest of the family of seven children of Mr. John Burrell, formerly of Cwmystwyth, and subsequently comptroller of N. M. Rothschild, bankers of London, and Mrs. Louisa Burrell, of Bryncrug, Towyn, Merionethshire. He was educated at Merchant Taylors' School, transferring from classics to science in 1906. He played a prominent part in school rugby and cricket and also represented the school at the public schools foils championship. In 1907 he won the major open science scholarship at University College, Oxford, together with one of the school exhibitions. While at Oxford (1907–10) he gained the coveted university prize in physiology and was awarded a half-blue for billiards. On leaving Oxford, he continued his studies at the London Hospital, and qualified M.R.C.S. and L.R.C.P. in 1915. Later in the same year he took the Oxford degrees of B.M., B.Ch., and subsequently passed the Primary Fellowship of the Royal College of Surgeons of England. He volunteered for service in the Royal Navy in the first world war and was commissioned as surgeon to H.M.S. *Princess Royal*, serving in this cruiser under Admiral Beattie at the battle of Jutland. Later he was transferred to Far Eastern waters in H.M.S. *Euryalus*. At the end of the war he was demobilized in China, where he entered private practice in Swatow, South China. In 1920 he returned to Wales and began his long and distinguished career as a general practitioner and surgeon at Aberystwyth.

P. J. writes: Dr. Charles Burrell was no ordinary man, but the unassuming possessor of many gifts. Exceptionally handsome, and of splendid physique, his very appearance commanded respect and admiration. His sense of humour, ready wit, and skill as a raconteur soon became widely appreciated among his friends, and his patients and colleagues alike quickly became aware that here, among them, was a man whose charm could not be denied. Gentleness and humanity were his also, and these gifts he used in his work as doctor and surgeon for over 30 years in

Cardiganshire and its neighbouring counties. His colleagues and the hospital nursing staffs with whom he worked all testified to his skill as a diagnostician, and to the wonderful work he did in surgery through the years, while those whom he looked after in general practice have reason always to remember his geniality, his invariable good humour, and the feeling they all had that his very presence at their side made them feel better. Always courteous and gentlemanly, he had countless friends. He enjoyed life, he worked and played hard, and he wasted no time. He died as he would have wished. Beloved by all, he was sustained throughout his career by the selfless devotion of his wife, to whom, and to his two daughters, we extend our sympathy and share in their sadness.

MARION W. DAVIES, M.B., Ch.B. D.P.H.

Dr. Marion W. Davies, assistant medical officer of health for maternity and child welfare at Stockport, died at Heaton Chapel on December 22, 1958. She was 51 years of age.

Marion Winifred Perry was born on May 18, 1907. She studied medicine at Manchester University, graduating M.B., Ch.B. in 1932. After house appointments at St. Mary's Hospital, Manchester, in the children's gynaecology and obstetrics departments, she proceeded to take the Manchester D.P.H. in 1935. In December, 1936, she married Dr. Arthur Davies, who was in general practice in Manchester. Unfortunately, after a short happy married life her husband died in July, 1937. She held temporary posts in the public health service in Manchester, Oldham, and Chadderton from 1936 to 1938, and did a year in general practice. She was a refractionist at Manchester Royal Eye Hospital from 1938 to 1941, when she joined the R.A.M.C. She served with distinction until December, 1945, being promoted staff captain, and receiving a mention in dispatches. On leaving the Army she was appointed assistant medical officer of health for maternity and child welfare in the county borough of Stockport in 1946, and occupied the post until her death. During this period she gained the love and esteem of everyone around her. Her fatal illness started in mid-year, and after an operation last September she returned to her own home. She died as she had lived, with great cheerfulness and fortitude. She is survived by her father and sister, to whom we extend our sincere sympathy.—J. Y.

W. F. J. WHITLEY, M.D., D.P.H.

Dr. W. F. J. Whitley, formerly county medical officer of health for Northumberland, died in hospital at Morpeth on November 4, 1958, two days after his 84th birthday.

William Frederic James Whitley was born on November 2, 1874, the son of a Bradford wool merchant, and was educated at Bradford Grammar School and at the Yorkshire College, Leeds. He then entered Edinburgh University, graduating M.B., Ch.B. in 1904, proceeding to the M.D. in 1917 with a commendation for his thesis. After graduation he held the appointments of assistant anaesthetist at Edinburgh Royal Infirmary, assistant medical officer at the Union Hospital, Bradford, and assistant medical officer at the Stafford County Asylum. He then moved to Morecambe, where he became honorary surgeon to the cottage hospital, and lecturer in first-aid and home nursing for the Lancashire County Council. Later he was appointed medical inspector of schools and an assistant medical officer under the county council, and while serving in this capacity he took the Oxford D.P.H. in 1910. Four years later he became deputy medical officer of health and tuberculosis officer for the county borough of Barrow-in-Furness, leaving there in 1916 to take up the appointment of medical officer of health for Swindon. There he was also medical superintendent of the Swindon and District isolation and smallpox hospitals. In 1920 he was appointed county medical officer of health for Northumberland, remaining in that post until 1940, when he retired. During the 20 years that he was in Northumberland he was particularly interested in the welfare of the blind and was responsible for the county council's scheme for the employment of home teachers. Throughout his career he was very active in the St. John Ambulance Brigade, and in the Venerable Order of St. John of Jerusalem he became successively a Serving Brother in 1938, an Officer in 1944, and a Commander in 1949. He was also interested in the work of the Boy Scouts, and was himself a member of the movement for many years. In 1933 he was elected a Fellow of the Royal Society of Edinburgh. Dr. Whitley was a widower, and he is survived by his son, Mr. J. M. Whitley, deputy clerk of the Salop County Council.

MAURICE MYERS, M.R.C.S., L.R.C.P.

Dr. Maurice Myers, who was deputy medical superintendent of Brompton Hospital Sanatorium, Frimley, died in the sanatorium on December 21, 1958. He had been in poor health for some months, but the end came suddenly and unexpectedly.

Born on June 7, 1897, Maurice Myers was a medical student at Durham University and at Guy's Hospital, from which he qualified M.R.C.S., L.R.C.P. in 1931. His early career was much interrupted by illness. He joined the staff of Brompton Hospital Sanatorium in 1932 and had worked there ever since. The life suited his restricted physical capacity, and in return he gave all he had to the hospital and to its patients. No one could have been a more loyal colleague, and he acquired great skill based upon wide experience in the treatment of tuberculosis. As a sanatorium physician Myers embodied the best traditions of the old school. Taught by R. C. Wingfield at a time when "for tuberculosis we prescribed not medicine but a way of life," his approach was bound to be autocratic, but he inspired great confidence in his patients. Beneath his somewhat gruff manner he concealed a deeply sensitive nature and a wealth of human kindness and sympathy, of which only his patients were fully aware. His untimely death at the age of 61 will be mourned not only by his friends who worked with him at Frimley but by countless ex-patients all over the world, to whom he gave himself unstintingly and who owe so much to his skill and understanding. He had only recently married, and our sympathy goes out to his wife in her bereavement.—A. F. F.-C.

G. E. LLOYD, *M.C.*, M.D., M.S.

Dr. G. E. Lloyd, who had practised in the Hexham district for over fifty years, died at his home in Hexham on December 4. He was 78 years of age and had remained in active practice until three months before his death.

George Errington Lloyd was born on February 28, 1880, the fifth child and third son of Henry Lloyd, J.P., of Lisheen Castle, Co. Tipperary, and of his third wife Louisa Jane, daughter of Minchin Jackson. He was educated at King's College, Dublin, and later at the University of Durham Medical College, Newcastle upon Tyne, where the family went to live after the death of Mr. Lloyd. As a student he showed a capacity above the average, obtaining honours in some of his professional examinations and winning prizes in many subjects. He played Rugby for the college and figured in many Dons Cup matches. After graduating M.B., B.S. in 1904, he filled the posts of accident room house-surgeon, house-surgeon to the late Mr. H. B. Angus, and house-surgeon to the ophthalmic and aural departments. He obtained the M.D., with gold medal, in 1913 with a thesis on heart block, the result of some original work on the polygraph, in which he had taken a special interest. In 1907 he joined Dr. D. Noel Jackson in practice at Corbridge-on-Tyne, where he worked until the outbreak of the first world war, when he transferred to Hexham to join Dr. J. A. Jackson in the family partnership in that

town. He had served with distinction in the R.A.M.C. during the war and was awarded the Military Cross in 1917 for attending to the wounded under fire while himself somewhat severely wounded. After returning to practice in Hexham, he continued his interest in surgery, performing many major operations in the local hospital, and in 1922 he obtained the degree of Master of Surgery, an unusual achievement for a general practitioner. Being well qualified in all branches of the art of medicine and surgery, and having a special interest in eye work, he was exceptionally well equipped to tackle all the problems confronting him in general practice. During the second world war, in addition to carrying on a busy general practice in the absence of his partner on military service, he found time to undertake the duties first as a member and subsequently as chairman of the National Service boards, work which he continued until the age of 70. Since the introduction of the National Health Service he had been a member of the ophthalmic services committee of the Northumberland Executive Council. He was chairman of the Hexham Division of the British Medical Association for twenty years (from 1928 to 1948), and on occasion its representative at the Annual Meetings. In his younger days he was a keen horseman, and rode regularly with the Tynedale hunt; latterly he devoted his energies to the pursuit of horticulture.

Dr. Lloyd was unassuming and somewhat reticent in manner, and his approach to patients was always quiet and unspectacular, but his kindliness, exceptional knowledge, and unruffled calm in the face of crisis endeared him to his patients, many of whom were quite unable to evaluate the versatile quality of the service he rendered. Endowed with a strong and wiry constitution, he remained active, physically and mentally, until his last illness, keeping well up to date by reading and attending meetings. He was twice married, first in 1905 to Victoria Hedley, of Tynemouth, who died in 1945, and secondly in 1946 to Alice Aitchison, who survives him. He is the last link with a race of doctors now mostly departed, and his passing will be grieved by all who knew him. Our sympathies are extended to his widow, married daughter, and grandchildren.—L. R. R.

DAVID LAMB, M.B., C.M., F.R.F.P.S.

Dr. David Lamb, formerly senior anaesthetist at the Victoria Infirmary, Glasgow, died at Teddington, Middlesex, on December 9, 1958. He was 88 years of age.

David Lamb was born on September 16, 1870. He graduated M.B., C.M., with high commendation, at Glasgow University in 1891, and after holding resident medical and surgical posts in the Western Infirmary, Glasgow, took up general practice in the steadily growing south side of the city. He lived for over fifty years in the suburb of Mount Florida. Although he did not enter the National Health Service in 1948 he continued to look after a few of his older patients until 1950, when he finally retired and moved with his wife to live in London. He was the senior member of the Glasgow Southern Medical Society, having been elected to it in 1896. He became president in 1913, and held this office during the years of the first world war till 1919. During some of this period he was president *in absentia*, because he served in France with the R.A.M.C. (T.A.) in the rank of major.

Dr. Lamb had a close association with the Victoria Infirmary, Glasgow, for nearly half a century. He was appointed anaesthetist in 1898, one of the first appointments of its kind to any Scottish hospital, and one which he held till 1922, when the increasing demands of his practice and his specialty became too great to allow as much time for hospital work as he felt it required. Nevertheless, he continued to give some anaesthetic assistance for many years thereafter. He was appointed by the Southern Medical Society as its representative on the board of governors of the Victoria Infirmary in 1925 and continued to serve in this capacity till 1946. He gave much helpful advice and wise counsel, and it was not without significance that during this period the anaesthetic service in the infirmary continued to march in the front rank of this developing specialty. He was elected F.R.F.P.S. in 1934. Although failing sight and hearing had much reduced his activity in the last year or so, his final illness was a brief one. He lost his wife, formerly Miss Ida Williams, in 1957 after some sixty years of marriage. He leaves two daughters, to whom our sympathy is extended.

H. P.-S. DEVITT, M.R.C.S., L.R.C.P.

Dr. H. Pye-Smith Devitt died on December 8 at Bournemouth, where he had been living for some years in retirement. He was 85.

Herbert Pye-Smith Devitt was a son of the late Sir Thomas Devitt, Bt., and was born in Upper Clapton on May 18, 1873. After education at Sherborne School and at Trinity College, Cambridge, he went to St. George's Hospital for his clinical studies and qualified in 1901. After completing house appointments at St. George's he started general practice at Rochester, and became assistant physician at St. Bartholomew's Hospital in that city. He had a rapid and marked success in practice, and after a few years removed to London, first practising in Bayswater and later in Grosvenor Street. He was a thoroughly competent general practitioner, fully up to the standards of his time. As he had also excellent address and genuine kindheartedness, his rapid strides and progress surprised none of his many friends. As a centre threequarter at Sherborne, at Trinity, and at St. George's he was a prominent Rugby footballer, and gained a Middlesex county cap. He was not very strong physically, not outstandingly fleet of foot, nor a long kicker; but he had a flair for the tactics of the game, bottomless pluck and energy, sold many more dummies than he bought, and was especially adept at coaching promising young players. He was three times married. His first wife, formerly Miss Roberta Anderson, died in 1934. They had two daughters and three sons, one of whom is a doctor. He married secondly Mrs. Muriel Blake, and after her death in 1951 he married Mrs. Carol Brownlee. Herbert Devitt never sought office in the councils of the B.M.A., but he served for some years on the Council of Epsom College. He was a member of the United Universities Club, and had been a member of the Cambridge Graduates Medical Club since 1903.

F.-J. VAN DE MEULEBROECK, M.D.

Dr. F.-J. van de Meulebroeck, a former burgomaster of Brussels, died on December 6 at the age of 82.

Fréderic-Joseph van de Meulebroeck was born at Laaken on November 17, 1876, and studied medicine at Brussels, where he graduated in medicine in 1901. He spent the next year in postgraduate study at hospitals in London.

During his student days Joseph van de Meulebroeck had devoted some of his time to the study of economics and political and social science. He soon deserted medicine for politics and entered the Liberal Party, being elected to the Council of Laaken in October, 1907. By 1911 he had become the mayor's right-hand man and was appointed *échevin* (deputy-mayor) responsible for education. His political career was interrupted by the war of 1914–18, in which he served with distinction as an army doctor. By 1921, when Laaken became part of Brussels, van de Meulebroeck had resumed his political career and became an alderman of the social department of Brussels. He played a large part in organizing the Brussels World Fair of 1935. During this period he also served for some years as a member of Parliament, representing the Liberals.

On November 28, 1939, van de Meulebroeck succeeded the famous Otto Max as burgomaster of Brussels. His proclamation in June, 1941, protesting against the removal of communal authority by the Germans, led to his arrest, and, although he was released after a few days, his

movements were restricted and he was obliged to live outside Brussels. At the end of the war he paid a visit to London as the guest of the Lord Mayor. He was given a barony in 1953 and resigned his office as burgomaster on February 10, 1956.

Medical Notes in Parliament

Parliament adjourned for the Christmas recess on December 18 and will reassemble on January 20. Before the adjournment the Government's Mental Health Bill was introduced in the Commons on December 17 and read for the first time. Its full title is: A Bill to repeal the Lunacy and Mental Treatment Acts, 1890 to 1930, and the Mental Deficiency Acts, 1913 to 1938, and to Make Fresh Provision with respect to the Treatment and Care of Mentally Disordered Persons and with respect to their Property and Affairs; and for Purposes connected with the Matters Aforesaid. The Bill is expected to receive its second reading on January 20.

Mental Defectives on Licence

Mr. N. DODDS (Erith and Crayford, Lab.) asked the Minister of Health on December 18 what progress had been made in reducing the lengthy periods during which mental defectives had normally been called upon to remain on licence when returned to the community; and what action was being taken to get rid of the condition forbidding any association with a member of the opposite sex during the period of licence. Mr. D. WALKER-SMITH stated that in 1956 hospitals were told that, save in exceptional circumstances, it should not be necessary for the period of licence to exceed twelve months. Information about the average length of licence was not available; but at the end of 1957 only 2,903 patients were on licence, compared with 4,493 at the end of 1955. The condition referred to in the second part of the question was included in Form L of the Schedule to the Mental Deficiency Regulations, 1948, but could be modified at the discretion of the superintendent and two members of the committee of management.

Informal Admission of Mental Defectives

Mr. DODDS asked what was the number of persons who had been admitted this year as voluntary patients into mental hospitals catering for mental defectives, up to the latest convenient date. Mr. WALKER-SMITH said he assumed that this referred to informal admissions to mental deficiency hospitals. As a result of the review which hospitals were asked to undertake last January, just over 22,000 hospital patients had been discharged from Order and readmitted on an informal basis. Information about the number of new admissions on this basis was not yet available.

Admissions on Certification

Mr. DODDS asked for the number of certified patients admitted to mental hospitals under the Lunacy Act and the Mental Deficiency Act, respectively, in 1957; and the comparable figures for 1950 and 1956. He was given the following information:

Year	Certified Patients Admitted to Designated Mental Hospitals	Mentally Defective Patients Admitted under Order to Mental Deficiency Hospitals
1950	18,891	3,164
1956	16,904	3,134
1957	14,126	3,135

The third column included Rampton Hospital, Moss Side Hospital, and the certified institutions.

The MINISTER OF HEALTH also told him that the average overcrowding in mental hospitals was 11.9% in England and Wales at the end of 1957. The figure at the end of 1956 was 14%.

Mr. DODDS asked how many persons over the age of 70, 80, and 90 years, respectively, had been certified for the first time and admitted to designated mental hospitals since January 1, 1957. Mr. WALKER-SMITH replied that the figures for 1957 were not yet available. The numbers of older certified patients admitted to designated mental hospitals during 1956 for the first time were: over 70, 3,485; over 80, 1,317; over 85, 429. The figures for those over 85 were included in the figures for those over 80, and both were included in the figures for those over 70.

Poliomyelitis

Mr. S. VIANT (Willesden West, Lab.) asked how many cases of poliomyelitis occurred in 1957 in persons who had been previously vaccinated; how many were under 15 years of age; how many were paralytic; and how many of the cases proved fatal. Mr. WALKER-SMITH stated that 32 cases of poliomyelitis were reported to the Department in 1957 in persons who had had two injections of vaccine. All were under 15 years of age. 16 were paralytic, and there was one death.

Mr. VIANT asked what were the circumstances in which all poliomyelitis vaccination was stopped recently in Denton, near Manchester, by the medical officer of health. Mr. WALKER-SMITH: I understand that on the occurrence of five cases of poliomyelitis with two deaths it was decided locally to postpone vaccinations. None of the patients had been vaccinated against poliomyelitis.

Domiciliary Consultations

Mr. DENIS HOWELL (Birmingham, All Saints, Lab.) asked what was the average number of domiciliary visits made each year by consultants participating in this scheme. Mr. WALKER-SMITH, in the following table, set out the numbers of consultants in contract with regional hospital boards for undertaking domiciliary consultations as at December 31; the number of domiciliary visits each year; and the average number of visits per consultant.

Year	Consultants	Domiciliary Visits	Average Visits per Consultant
1950	4,916	153,267	31·2
1951	5,129	162,201	31·6
1952	5,457	177,812	32·6
1953	5,551	200,143	36·1
1954	5,489	218,104	39·7
1955	5,681	231,377	40·7
1956	5,846	258,981	44·3
1957	5,945	279,474	47·0

Sex Bar for Hospital Post

Dame IRENE WARD (Tynemouth, Con.) asked the Minister whether, in view of a recent advertisement from a London teaching hospital of a post specified only for men, he would state the policy of the Government with regard to sex discrimination in selection for hospital appointments. Mr. WALKER-SMITH: It is considered that as a general rule applications for hospital appointments should be invited from suitably qualified applicants of either sex. It is recognized, however, that special circumstances may make it advisable to invite applications for certain posts from members of one sex only.

Health Service Charges

The MINISTER OF HEALTH informed Mr. GRESHAM COOKE (Twickenham, Con.) on December 10 that the estimated annual cost to the Exchequer of abolishing the Health Service charges on prescriptions, dental treatment, and spectacles would be about £24m., after taking into account the refunds made in certain cases but without making any allowance for any increase in the numbers of prescriptions, dental treatments (including the provision of dentures), or spectacles which might result. The approximate annual cost of setting up a free chiropody service for the aged would be over £1m.

Notification of Burns and Scalds

MR. SOMERVILLE HASTINGS (Barking, Lab.) asked if the Minister of Health would give instructions that the name and address of every child under 10 years of age admitted to hospital for burns and scalds should be at once communicated to the M.O.H. of the locality so that advice as to the prevention of such accidents might be tendered to those responsible. MR. R. THOMPSON stated that the Ministry had already asked hospital authorities to co-operate with M.O.H.s by supplying them with certain information about persons of any age requiring hospital treatment as a result of accidents in the home.

Poliomyelitis in Scotland.—By the end of October 735,000 people had been given poliomyelitis vaccination in Scotland, and the vaccination of an additional 113,000 who had been registered was proceeding.

Medico-Legal

CORONER'S PROCEDURE IN HOMICIDE

[FROM A MEDICO-LEGAL EXPERT]

A recent case in which a mother was charged with the murder of her child (*Manchester Guardian*, November 5) illustrates some points in coroner's procedure when the charge is homicide. A child aged 3 months was found dead in a cot in its parents' room. The face was bruised and necropsy showed effused blood in the scalp, in the subdural space, and on the surface of the brain. There were old, healed rib fractures of a month's duration, and there was generalized pallor indicating anaemia.

The coroner opened an inquest, taking evidence of discovery and of identification. The mother was charged with murder, acquitted at Assizes, and discharged. At her trial no medical evidence was taken.

The coroner then resumed his inquest for the purpose of taking medical evidence. The opinion of the pathologist who made the first examination was heard. He thought the facial bruises were traumatic and that death was the result of concussion and cerebral contusion from head injury. A pathologist of great forensic experience carried out a post-mortem examination two days after the first one. He agreed the facial bruising was traumatic and consistent with marks caused by fingers, by hard pressure, or striking. Clot from the superior sagittal sinus showed organization and had formed at least 12 hours before death. He confirmed the anaemia and said it had given rise to non-traumatic sagittal sinus thrombosis, recognized as occurring in children with anaemia who have suffered bouts of ill-health. There was evidence of external injury, but not enough to account for the cerebral contusion. He thought death was due to non-traumatic superior sagittal sinus thrombosis.

The first pathologist agreed that this opinion was reasonable; and the coroner recorded the medical cause of death and said the case was adjourned and would not be resumed.

Coroner's Duty

A coroner's first duty is to obtain details enabling death to be registered. These include date and place of death, name, age, sex, occupation, and the cause of death. A medical cause of death can be certified by two persons only—the doctor in attendance during the last illness or the coroner. When it seems that death comes from a criminal act the coroner opens an inquest and takes registrable particulars only. He then adjourns the hearing. If a person is charged, the clerk to the appropriate court officially notifies the coroner of the result of the criminal proceedings. The coroner then has power further to adjourn, and not resume, the inquest (Coroners (Amendment) Act, 1926, section 20).

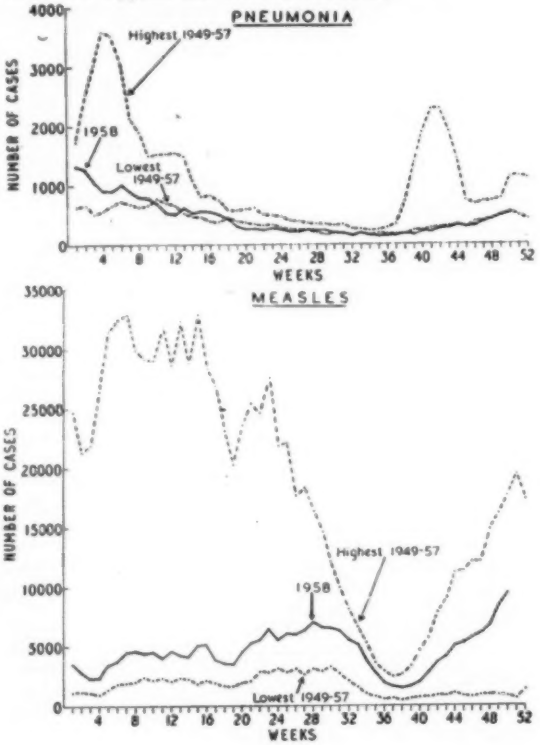
If the person responsible for the homicide is not found the coroner takes the evidence in full before a jury, who give a verdict of, for example, murder by person or persons unknown. This is recorded on the coroner's certificate after inquest and sent to the Registrar of Deaths. The point of the procedure is that the issue of homicide is not tried in two separate courts. In any case, the only person who can supply the Registrar with the required information is the coroner.

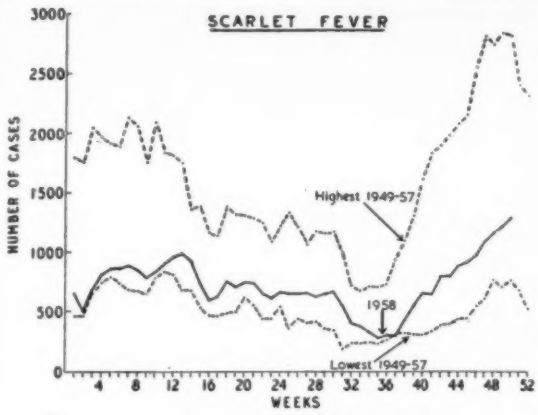
Usually the medical cause of death is taken when the inquest is opened. It is given in a short form with a view to ultimate registration and confined to such statement as "haemorrhage from stab wounds of the chest." No interrogation of the pathologist is made. There may be reasons, however — for example, lengthy histological examination—why the medical cause of death is not taken when the inquest is opened. In such circumstances this information may be given on oath at any time after the inquest is opened, though the proceedings must be formally resumed in public. It must be given eventually, however, to enable the coroner to complete his certificate. Usually in alleged homicide medical evidence beyond the simple cause of death is not heard by the coroner; though, sometimes, there may be circumstances when, in the interests of justice, it is desirable for him to do so.

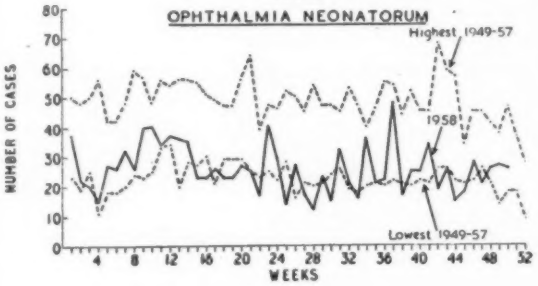
Vital Statistics

Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of certain diseases notified weekly in England and Wales. Highest and lowest figures reported in each week during the years 1949–57 are shown thus - - - - - -, the figures for 1958 thus ———. Except for the curves showing notifications in 1958, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.







Week Ending December 13

The largest fluctuations in the numbers of notifications of infectious diseases in England and Wales during the week ending December 13 were increases of 1,064 for measles, from 8,382 to 9,446, 188 for dysentery, from 1,020 to 1,208, and 75 for scarlet fever, from 1,217 to 1,292; the only large decrease was 108 for whooping-cough, from 749 to 641.

The rise in the incidence of measles was highest in the southern section of the country; the largest increases were 167 in Middlesex, from 462 to 629, 142 in Somersetshire, from 144 to 286, 119 in Essex, from 260 to 379, 118 in Wiltshire, from 301 to 419, 106 in Derbyshire, from 143 to 249, and 97 in Surrey, from 270 to 367; the only large exception to the general increasing trend was a fall of 70 in Staffordshire, from 370 to 300. The largest fluctuation in the trends of scarlet fever was a fall of 25 in Staffordshire, from 62 to 37. The largest decrease in the number of notifications of whooping-cough was 21 in Northamptonshire, from 30 to 9. 2 cases of diphtheria were notified, being 2 fewer than in the preceding week.

The notifications of acute poliomyelitis numbered 47, and these were 10 fewer for paralytic and 4 more for non-paralytic cases than in the preceding week. The largest returns were Lancashire 11 (Burnley C.B. 3, Liverpool C.B. 3), Yorkshire West Riding 6 (Huddersfield C.B. 2, Leeds C.B. 2), London 4 (Wandsworth 3).

The chief centres of dysentery during the week were Yorkshire West Riding 219 (Leeds C.B. 62, Earby U.D. 62, Huddersfield C.B. 43, Barnsley C.B. 17), Glamorganshire 189 (Cardiff C.B. 142, Rhondda M.B. 27, Llantrisant and Llantwit Fardre R.D. 11), London 105 (Battersea 24, Islington 10, Lewisham 10), Lancashire 91 (Eccles M.B. 22, Liverpool C.B. 21, Manchester C.B. 19), Warwickshire 88 (Coventry C.B. 70, Birmingham C.B. 14), Middlesex 66 (Hendon M.B. 46), Essex 51 (Rochford R.D. 16, East Ham C.B. 11), Cumberland 40 (Carlisle C.B. 20), Northumberland 34 (Ashington U.D. 16), Kent 29 (Maidstone R.D. 12), Surrey 27 (Croydon C.B. 10), Berkshire 27 (Maidenhead M.B. 25), Durham 27, Nottinghamshire 26 (East Retford R.D. 13), Yorkshire East Riding 25 (Kingston upon Hull C.B. 19), Staffordshire 21, Wiltshire 21 (Swindon M.B. 13).

INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending December 13 (No. 50) and corresponding week 1957.

Figures of *cases* are for the countries shown and London administrative county. Figures of *deaths* and *births* are for the whole of England and Wales (London included), London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES	1958 Eng. & Wales	1958 Lond.	1958 Scot.	1958 N. Ire.	1958 Eire	1957 Eng. & Wales	1957 Lond.	1957 Scot.	1957 N. Ire.	1957 Eire
Diphtheria ..	2	1	6	0		3	1	2	0	
Dysentery ..	1,208	105	169	9	4	669	121	128	12	2
Encephalitis, acute	7	0		0		0	0		0	
Enteric fever:										
Typhoid ..	2	0	0	0	1	0	0	1	0	
Paratyphoid ..	2	0	2(B)	0	1(B)	11	0	1(B)	0	2(B)
Food-poisoning ..	164	20	9	2		128	5	21	1	
Infective enteritis or diarrhoea under 2 years				5	35				5	25
Measles*	9,446	633	132	50	419	2,450	40	49	44	8
Meningococcal infection	19	0	6	0	1	34	1	5	0	1
Ophthalmia neonatorum	26	7	2	0		19	1	1	0	
Pneumonia† ..	520	37	304	3	2	778	52	354	9	21
Poliomyelitis, acute:										
Paralytic ..	31	3	} 4	0	3	{ 53	0	} 4	0	4
Non-paralytic ..	16	1				18	0			
Puerperal fever‡ ..	187	37	8	0		233	62	2	2	
Scarlet fever ..	1,292	92	101	30	31	794	50	62	20	17
Tuberculosis:										
Respiratory ..	455	53	107	17		507	58	102	22	
Non-respiratory	55	8	9	4		45	2	14	1	
Whooping-cough	641	29	68	92	113	504	23	38	3	6

DEATHS	1958 Eng. & Wales	1958 Lond.	1958 Scot.	1958 N. Ire.	1958 Eire	1957 Eng. & Wales	1957 Lond.	1957 Scot.	1957 N. Ire.	1957 Eire
Diphtheria ..	1	0	0	0	0	No comparable figures available.	0	0	0	0
Dysentery ..	0	0		0			0		0	
Encephalitis, acute		1			0		0			0
Enteric fever ..	0	0	0	0			0	0	0	
Infective enteritis or diarrhoea under 2 years	8	1	0	0	0		0	0	1	2
Influenza	33	1	2	0	1		16	2		6
Measles		0	0	0	1		0	0	0	0
Meningococcal infection		0	0				0	0		
Pneumonia ..	704	46	29	14	15		105	24	20	16
Poliomyelitis, acute	3	0		0	0		0		0	0
Scarlet fever ..		0	0	0	0		0	0	0	0
Tuberculosis:										
Respiratory ..	} 117	{ 7	8	0	6		16	11	0	7
Non-respiratory		4	0	0	0		4	0	0	0
Whooping-cough ..	0	0	0	0	0		0	0	0	0
Deaths 0–1 year ..	343	23	30	5	9		35	26	16	10
Deaths (excluding stillbirths) ..	11,758	921	738	129	195		1212	711	124	172
LIVE BIRTHS ..	13,510	1215	916	218	303		1089	943	227	291
STILLBIRTHS ..	310	18	29				28	17		

* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenzal pneumonia.
‡ Includes puerperal pyrexia.

Medical News

Royal College of Surgeons.—A sum of £150,000 from Mr. G. A. VANDERVELL, for the endowment of the College's Chair of Pharmacology, was gratefully received by the council of the Royal College of Surgeons, meeting on December 11 under the chairmanship of Sir JAMES PATERSON ROSS. Mr. Vandervell is the industrialist responsible for the development of the Vanwall racing car. The Council appointed Lord COHEN OF BIRKENHEAD as the first Watson-Jones lecturer, Mr. A. DICKSON WRIGHT Bradshaw lecturer for 1959, and Professor R. N. BRADLAW Menzies Campbell lecturer. A Moynihan lectureship was awarded to Professor ENGLEBERT DUNPHY, of Harvard Medical School, and the Begley prize was presented to Miss M. E. ASHWORTH, of Charing Cross Hospital Medical School. The diploma of F.R.C.S. was granted to the following successful candidates:

D. A. Dawson (otol.), J. G. B. Myles, O. O. F. Ffooks (oph.), J. Ransome (otol.), M. J. Ball, K. M. Bryant, B. Altman, N. E. Shaw, M. S. Robertson (otol.), J. C. Smith, F. E. Loeffler, J. W. Wilson, M. V. Naidu, E. G. Hardy, A. A. Asirvatham, M. S. Beare, P. M. Chaudhuri, (oph.), M. Kumarasinhe, B. C. Mukerjee W. J. Oram, S. Sen, S. K. Das, D. N. P. Yadava, D. G. Bonham, J. R. Chanmugam, G. H. Dunstone, D. K. Kabraji, J. Mander, S. J. Seevaratnam, B. C. M. Chester, J. H. Neame (otol.), B. R. Parekh, F. Shah, P. A. Shah (otol.), P. R. Casson, D. S. Gill, D. J. Grimsdell, E. D. Morris, J. R. Pearson, L. J. Pigott (oph.), M. K. A. Youssef, W. L. H. Armstrong, G. Birbara, I. Cher (oph.), H. W. M. Collymore, M. Hobsley, H. K. Ismail (otol.), G. R. W. Latham, R. J. Ryall, G. F. Walker, C. Baneriee, E. G. Bennet, D. O. Hancock, R. L. Hucksten, V. B. Jhaveri, N. M. Lalliee, D. G. Macleish, B. T. Nayar, W. S. E. Perera, P. F. Plumley, A. J. Rollo, J. G. Sallis, P. Sharma, W. C. Shirer, H. G. Watts, E. C. Wood, C. I. Woolf, S. V. Anand, S. K. Bhansali, D. B. Bower, J. L. Castle, V. J. L. Cullum, H. M. El-Sayed, H. Green, V. C. James, J. L. Jardine, T. R. Kapur, D. M. Llewelyn, P. F. Lynch, A. Mann, S. J. Mehta, J. D. H. Muir, M. Srinivasan, S. Y. Taktak, H. Thomas, A. M. Alimumal, M. W. Brown, J. K. A. Clezy, M. J. Joshi, R. E. Kemp, A. R. Patel, M. E. Shackleton, O. H. Shaheen (otol.), L. N. Vora, K. M. Burkill, J. S. T. Cox, F. Ehrlich, S. Subramanian, J. Vinnicombe, and B. K. Vohra.

B.M.A. Film Competition.—The winners of last year's competition for 16-mm. medical films were:—*Non-Commercial Category*: First prize.—"The Treatment of Cardiac Arrest" (colour, sound, 9 min.), Sir RUSSELL BROCK and the department of medical illustration, Guy's Hospital Medical School. Awards of merit.—"Correction of Uniocular Aphakia by Anterior Chamber Acrylic Implants" (colour, silent, 16 min.), Mr. D. P. CHOYCE and the department of medical photography, General Hospital, Southend-on-Sea; and "A Ptosis Operation" (colour, silent, 13 min.), Mr. H. B. STALLARD and the medical illustration department, Institute of Ophthalmology. *Commercial Category*: First prize.—"The Management of Twins in Pregnancy and Labour" (colour, sound, 22 min.), Professor W. C. W. NIXON and Mr. W. G. MACGREGOR with the Wellcome Film Unit. Award of merit.—"Cardiac Arrest" (colour, silent, 16 min.), Dr. J. BEARD, a "Verity Film" for Imperial Chemical Industries Ltd. Details of the Association's 1959 medical film competition will be announced later.

King Edward's Hospital Fund for London.—At a meeting of the Fund's general council on December 10, the DUKE OF GLOUCESTER drew attention to the role of the day hospital in the care of the elderly. The Fund had just made a grant of £25,000 towards a day hospital in the grounds of St. Luke's Hospital, Chelsea, he said. It was also offering £50,000 towards the conversion of a derelict block at St. Clement's, Bow, into a day hospital and treatment centre, with two wards above, for mentally disturbed old people. The council earmarked £390,000 for grants to hospitals and convalescent homes and for the Fund's advisory services and educational activities in 1959.

Travelling Scholarship for G.P.s.—Details of a travelling scholarship offered by the trustees of the Claire Wand Fund are printed in the Association Notices this week (*Supplement*, p. 7). The purpose of the scholarship is to enable a general practitioner to study what is done for the further education of general practitioners in Canada and the U.S.A. The last date for the submission of applications is January 31.

Royal Masonic Hospital.—QUEEN ELIZABETH THE QUEEN MOTHER opened a new extension—the Wakefield Wing—at the Royal Masonic Hospital on December 10. The cost of the new wing, which will provide an extra 80 beds, is put at about £750,000.

Lecture for Schoolchildren.—The Royal College of Surgeons broke new ground when on December 29 it held a Christmas-holiday lecture for schoolchildren. The idea was suggested by a 14-year-old schoolboy, and the lecture was given at the College by Sir HENEAGE OGILVIE. He spoke on "The Romance of Surgery." In view of the success of this venture, further holiday lectures may be arranged.

A.D.G., W.H.O.—Dr. N. I. GRASHCHENKOV has succeeded Dr. W. A. TIMMERMAN as one of the three assistant directors-general of W.H.O. Dr. Grashchenkov is a Russian neurologist. In 1938 he became professor of neurology at the first Moscow Medical Institute, and in 1955 he was appointed chairman of the Medical Research Council of the U.S.S.R. Ministry of Health. At W.H.O. he will be concerned particularly with the programmes on biology and pharmacology, health, and vital statistics, and editorial and reference services.

Queen's University, Belfast.—Mr. R. B. WELBOURN, the reader in surgery, has been appointed to a personal chair in surgical science. Mr. Welbourn was educated at Cambridge and Liverpool Universities, graduating in medicine in 1942. Before going to Belfast he held surgical research appointments at Liverpool and was also a Mayo Foundation fellow. Dr. P. C. ELMES has been appointed to a lectureship in therapeutics and pharmacology, Dr. W. G. MILLAR to a lectureship in midwifery and gynaecology, and Dr. G. C. R. CAREY to a lectureship in preventive medicine.

Edinburgh University.—At a meeting of the university court on December 15 Mr. A. N. SMITH was appointed lecturer in clinical surgery and Mr. N. L. STOKOE lecturer in ophthalmology.

"Brit. J. Tuberc."—The title of the *British Journal of Tuberculosis and Diseases of the Chest* has now been changed to *British Journal of Diseases of the Chest.*

Medical M.P.—Mr. SOMERVILLE HASTINGS (Barking, Lab.) has announced that he will not stand for Parliament at the next General Election. He first entered Parliament in 1923, representing Reading. He was born in 1878.

Medical Golfing Society.—The annual dinner was held in London on December 4. Dr. S. POPE was elected president and Dr. J. PARK captain for 1959.

COMING EVENTS

Institute of Dermatology.—Semi-permanent exhibition, January 5–24, on "Diseases of the Nails."

B.B.C. Television.—"Medico," a dramatized documentary of the G.P.O.'s medical advice service for ships at sea, January 7, 9.15 to 10 p.m.

Watson Smith Lecture.—Dr. H. R. VICKERS will lecture on "The Place of Dermatology in a General Hospital" on January 13 at 5 p.m. at the Royal College of Physicians of London.

Clinical Trials.—A symposium on "Progress in the Evaluation of Drugs," sponsored by the Association of the Medical Advisers in the Pharmaceutical Industry, will be

held on January 22 at the Royal Society of Medicine (2.15–6.30 p.m.). Tickets (free) are obtainable from Dr. E. T. KNUDSEN, c/o Royal Society of Medicine, 1, Wimpole Street, London, W.1.

Ninth International Congress of Radiology.—In Munich, July 23–30. Details from the Congress Secretariat, 29, Reitmorstrasse, Munich, 22.

NEW ISSUES

The journals listed below are obtainable from the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1.

British Journal of Ophthalmology.—Issued monthly (£6 annually). The new issue (Vol. 42, No. 12) includes:

EXPERIMENTAL TRACHOMA PRODUCED BY CULTURED VIRUS. L. H. Collier, S. Duke-Elder, and B. R. Jones.
ACCIDENTAL LABORATORY INFECTION WITH TRACHOMA. C. H. Smith.
CATARACT EXTRACTION UNDER GENERAL ANAESTHESIA. J. Gibson Moore.
ROBERT BOYLE'S "UNCOMMON OBSERVATIONS ABOUT VITIATED SIGHT" (LONDON, 1688). R. A. Hunter and F. Clifford Rose.
EFFECT OF DIAMOX ON PLASMA BICARBONATE AND ON THE ELECTROLYTE BALANCE IN RELATION TO INTRA-OCULAR PRESSURE IN MAN. D. Campbell, N. E. A. Renner, and E. Tonks.
NEW METHOD OF OPERATION FOR DETACHMENT OF THE RETINA WITH TEARING OF THE MACULA LUTEA. M. Madroszkiewicz.
RETINAL DETACHMENT AT THE POSTERIOR POLE. C. I. Phillips.
TEAR GLUCOSE IN DIABETICS. J. G. Lewis and P. Stevens.
FUNDUS CHANGES IN UVEO-MENINGITIS. P. Sivasubramaniam.
FIXATION IN PERIMETRY AND CAMPIMETRY. H. Lytton.

Thorax.—Issued four times a year (£3 annually). The new issue (Vol. 13, No. 4) includes:

THE TECHNIQUE OF SURGICAL CORRECTION OF ANOMALIES OF THE PULMONARY VEINS IN A SERIES OF 25 CASES. F. Risch and Chs. Hahn.
THE OPERATION AND MANAGEMENT OF A CASE AFTER DIVERSION OF THE INFERIOR VENA CAVA INTO THE LEFT ATRIUM AFTER THE OPEN REPAIR OF AN ATRIAL SEPTAL DEFECT. V. O. Björk, L. Johansson, B. Jonsson, O. Norlander, and B. Nordenström.
THE RELATION OF MEDIAL THICKNESS OF SMALL MUSCULAR PULMONARY ARTERIES TO IMMEDIATE POSTNATAL SURVIVAL IN PATIENTS WITH VENTRICULAR SEPTAL DEFECT OR PATENT DUCTUS ARTERIOSUS. Donald Heath, H. J. C. Swan, James W. DuShane, and Jesse E. Edwards.
ABSENT LEFT PULMONARY ARTERY AND RIGHT-SIDED AORTIC ARCH IN EISENMENGER'S COMPLEX. H. A. Fleming.
FIRST EXPERIENCES IN THE CLINICAL USE OF EXTRACORPOREAL CIRCULATION. A. G. Brom and J. Nauta.
OSSIFYING BRONCHIAL ADENOMA. Sir Clement Price Thomas and A. D. Morgan.
TUMOURS AND CYSTS OF THE MEDIASTINUM. Ian M. Morrison.
AMYLOIDOSIS OF THE LOWER RESPIRATORY TRACT. C. Barrington Prowse.
PULMONARY TELANGIECTASIS. Vincent Powell.
BRONCHIOLITIS FROM NITROUS FUMES. Christopher S. Darke and A. J. N. Warraes.
PLASMA ELECTROLYTE CHANGES IN HYPOTHERMIA. K. A. Munday, G. F. Blane, E. F. Cain, and E. S. Machell.

Archives of Disease in Childhood.—Issued six times a year (£4 4s. annually). The new issue (Vol. 33, No. 172) includes:

THE FLUID SHIFT FROM THE VASCULAR COMPARTMENT IMMEDIATELY AFTER BIRTH. Douglas Gairdner, John Marks, Janet D. Roscoe, and R. O. Brettell.
THE PLASMA AMINO ACIDS IN MALNUTRITION: PRELIMINARY OBSERVATIONS. Roland G. Westall, Ellen Roitman, Carmen de la Peña, Howard Rasmussen, Joaquin Cravioto, Federico Gomez, and L. Emmett Holt, Jr.
HYPOCALCAEMIC TETANY DEVELOPING WITHIN 36 HOURS OF BIRTH. W. S. Craig and M. F. G. Buchanan.
CELLULAR IMMUNITY AT BIRTH: THE MECHANISM AND NATURE OF THE PHAGOCYTIC RESPONSE. M. S. Edwards, L. L. Griffiths, and P. N. Swift.
THROMBOTIC MICROANGIOPATHIC HAEMOLYTIC ANAEMIA. M. J. Robinson, N. P. Orchard, and A. R. Eden.
ACUTE ACQUIRED HAEMOLYTIC ANAEMIA ASSOCIATED WITH HERPES SIMPLEX INFECTION. R. McLaren Todd and N. V. O'Donohoe.
HAEMOLYTIC ANAEMIA IN A CHILD RECEIVING NITROFURANTOIN. David Levy and Alice Porteus.
ERYTHROCYTE SEDIMENTATION RATE, C-REACTIVE PROTEIN DETERMINATION, SERUM PROTEIN FRACTIONS, FIBRINOGEN LEVEL, AND ANTISTREPTOLYSIN REACTION IN 52 RHEUMATIC CHILDREN. N. Popov and S. Stanisheva.
THE PROGNOSIS OF IDIOPATHIC RENAL ACIDOSIS IN INFANCY WITH OBSERVATIONS ON URINE ACIDIFICATION AND AMMONIA PRODUCTION IN CHILDREN. Elizabeth U. Buchanan and G. M. Komrower.
DIASTEMATOMYELIA. C. C. Michael James and L. P. Lassman.
A CASE OF CUSHING'S SYNDROME IN AN INFANT. E. Goldblatt and A. H. Snaith.
EPIDEMICS OF GASTRO-ENTERITIS ASSOCIATED WITH ESCH. COLI O119 INFECTION. K. Hugh-Jones and G. I. M. Ross.

Ophthalmic Literature.—The new issue (Vol. 12, No. 2) is now available. It contains a comprehensive selection of abstracts of the literature on ophthalmology and related subjects. Six issues and a volume index each year published at quarterly intervals; annual subscription £4 4s. (or in combination with *British Journal of Ophthalmology* £9).

Abstracts of World Medicine.—Issued in the first week of each month, this journal contains abstracts of important papers selected from the current medical literature of the world. Annual subscription £4 4s.

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Application should be made first to the institution concerned.

Sunday, January 4

UNIVERSITY COLLEGE HOSPITAL.—10.15 a.m., meet in Front Hall of main Hospital. Lecture-demonstration for general practitioners. Clinical demonstration by Mr. H. R. I. Wolfe: Some Disorders of the Small Intestine.

Wednesday, January 7

INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., Dr. R. V. Gibson: Radiology of the Heart.
INSTITUTE OF LARYNGOLOGY AND OTOLOGY.—5.30 p.m., Dr. I. Friedmann, Dr. D. A. Osborn, and Dr. A. L. Jeancs: clinical pathological conference.
POSTGRADUATE MEDICAL SCHOOL OF LONDON.—2 p.m., Professor J. H. Dible: Medical Illustration.
● SOCIALIST MEDICAL ASSOCIATION.—7.15 p.m., Dr. J. P. Martin, Ph.D.: Prescribing in the Health Services—A Survey of Practice and Policy.

Thursday, January 8

LIVERPOOL MEDICAL INSTITUTION.—Joint meeting with Liverpool Paediatric Club, 8 p.m., Mr. P. P. Rickham and Dr. J. R. Roberts: Recent advances in the Management of Hydrocephalus.
ROYAL COLLEGE OF SURGEONS OF ENGLAND.—5 p.m., Hunterian Lecture by Professor R. A. Moore: Congenital Anomalies of the Urinary Tract in Relation to Disorders of Micturition.
ST. GEORGE'S HOSPITAL MEDICAL SCHOOL.—5 p.m., Dr. Desmond Curran: Psychiatry.
UNIVERSITY COLLEGE LONDON: DEPARTMENT OF ANATOMY AND EMBRYOLOGY.—At Anatomy Theatre, Gower Street, W.C., 5.30 p.m., public lecture by Dr. Harry Grundfest (New York): Pharmacology of Cerebral Synapses.

Friday, January 9

CAMBRIDGE UNIVERSITY POSTGRADUATE MEDICAL SCHOOL.—At Radiotherapeutic Centre, Addenbrooke's Hospital, 4 for 4.15 p.m., clinico-pathological conference. Dr. Sheila Sherlock: Liver Disease.
INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., Dr. N. C. Oswald: clinical demonstration.
INSTITUTE OF LARYNGOLOGY AND OTOLOGY.—3.30 p.m., clinical discussion for general practitioners by Mr. J. C. Hogg: Nasal Obstruction.
INSTITUTION OF ELECTRICAL ENGINEERS: MEDICAL ELECTRONICS DISCUSSION GROUP.—A, Savoy Place, W.C., 5.30 for 6 p.m., discussion to be opened by Dr. M. H. Evans and Dr. G. B. B. Chaplin: Physiologists' Requirements for D.C. Amplifiers.
POSTGRADUATE MEDICAL SCHOOL OF LONDON.—(1) 10 a.m., Mr. D. A. Bailey: Infections of the Hand. (2) 4 p.m., Dr. R. E. Bonham-Carter: Treatment of Cardiac Failure in Infants.

Saturday, January 10

CAMBRIDGE UNIVERSITY MEDICAL SCHOOL.—At Addenbrooke's Hospital, Symposium on Emergencies in General Practice. Morning: 10.30 a.m., Mr. W. S. Lewin: Acute Head Injury; 11.30 a.m., Mr. B. McN. Truscott: Perineal Pain, Pus, and Piles; 12.15 p.m., Mr. K. F. Wilsdon: E.N.T. Emergencies. Afternoon: 2.30 p.m., Dr. M. J. Greenberg: Acute Respiratory Disorders; 3.15 p.m., Dr. G. F. Wright: Ocular Emergencies.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Bell.—On December 20, 1958, at the Louise Margaret Maternity Home, Aldershot, Hants, to Sheila, wife of Major R. L. Bell, R.A.M.C., a daughter—Brigid Mary.
Lynn.—On December 18, 1958, at Rush Green Hospital, Romford, Essex, to Constance, wife of Dr. Conrad Lynn, a sister for Jonathan—Judith.
Mercer.—On November 28, 1958, at Huddersfield, Yorks, to Dr. and Mrs. M. H. Mercer, of Croft House, Meltham, Yorks, a sister for Nigel and Nicholas—Lucy Elizabeth.

DEATHS

Alderman.—On December 11, 1958, at "Norbury," Purton, Wilts, George Walkley Alderman, M.R.C.S., L.R.C.P., aged 48.
Davies.—On December 22, 1958, at 263, Wellington Road North, Heaton Chapel, Stockport, Cheshire, Marion Winifred Davies, M.B., Ch.B., D.P.H.
Fox.—On December 27, 1958, at Bermondsey Medical Mission, 44, Grange Road, London, S.E., Selina FitzHerbert Fox, M.D., aged 87.
Green.—On December 21, 1958, at Beechleys, Winkton, Christchurch, Hants, Vincent Green, M.D., F.F.Hom., late of Wimbledon, London, S.W., aged 88.
Legge.—On December 21, 1958, at Bristol, Sydney Colen Legge, M.R.C.S., L.R.C.P., formerly of Forcaste Street, Worcester, aged 88.
McDonald.—On December 20, 1958, in Edinburgh Royal Infirmary, James Walter McDonald, M.B., Ch.B., of 41, Stirling Road, Edinburgh.
McEachran.—On December 11, 1958, at his home, Duncan McEachran, M.B., Ch.B., of Edinburgh.
McLagan.—On December 25, 1958, at St. Mary's Hospital, London, W., Francis McLagan, M.B., M.R.C.P., D.P.M., D.T.M.&H., of Sark, Channel Islands, formerly of Gold Coast, West Africa, and Sierra Leone.
Martin.—On December 18, 1958, Robert Telford Martin, M.R.C.S., L.R.C.P., of Vicarage Cottage, Dersingham, King's Lynn, Norfolk.
Meighan.—On December 6, 1958, at sea, John Spence Meighan, M.B., Ch.B., of 26, Downleaze, Bristol.
Myers.—On December 21, 1958, at Brompton Hospital Sanatorium, Frimley, Aldershot, Hants, Maurice Myers, M.R.C.S., L.R.C.P.
Newton.—On December 17, 1958, in a nursing-home, William Henry Newton, M.B., B.Ch., of Walmer, Kent, aged 80.
Nicoll.—On December 17, 1958, in a nursing-home, James Nicoll, M.D., D.P.H., of 26, Maridon Road, Shiphay, Torquay, Devon.
Perkins.—On December 17, 1958, in hospital, Ringwood, Hants, Herbert Edward Perkins, M.R.C.S., L.R.C.P., Surgeon Captain, R.N. (retired), late of Ascension Island.
Proudfoot.—On December 17, 1958, at 467, Whirlowdale Road, Sheffield, Yorks, Robert Proudfoot, M.D., D.P.H.
Robinson.—On December 6, 1958, at St. Thomas's Hospital, London, S.E., James Albert Robinson, M.R.C.S., L.R.C.P., of Clapham, London, S.W.

Any Questions?

We publish below a selection of those questions and answers which seem of general interest. It is regretted that it is not possible to supply answers to all questions submitted.

Strontium-90 Absorption

Q.—*Are there any measures which might be taken to reduce absorption, particularly by infants, of strontium-90 from contaminated natural sources?*

A.—There is no medical indication at present for trying to reduce the absorption of strontium-90 from contaminated natural sources, even in infants. A level of contamination at which measures should be taken might follow nuclear warfare or a localized accident of considerably greater magnitude than, or of a different kind from, the 1957 accident at Windscale. The administrative action to be taken would then be decided on a national scale, and clearly suckling infants and growing children should have first claim on supplies of safe cow's milk if these were limited in quantity. Milk powder, or preserved liquid milk, already manufactured from safe supplies, is the natural substitute for contaminated fresh cow's milk. Supplementary feeding with additional calcium is not likely to be of more than marginal benefit, since doubling the daily intake of calcium would not be expected to do more than halve the retention of strontium. Too much calcium may have undesirable side-effects of its own. Flour in this country is already fortified with calcium derived from mined limestone and hence free from radioactive strontium.

Incidence of Whooping-cough

Q.—*What are the incidence, overall mortality, and case mortality for whooping-cough in Britain at ages under 1 year, 1–4 years, 5–14 years, and over 14 years?*

A.—Although whooping-cough is a notifiable disease, notifications are notoriously incomplete. It is thus impossible to make accurate estimates of national rates of incidence and case fatality for the disease. From the reports summarized in the Registrar General's Annual Review for 1956,[1] the following attack rates, case-fatality rates, and death rates can be computed to give some indication of current patterns in relation to age and sex.

Age	Attack Rate (per 1,000 p.a.)		Case Fatality Rate (per 100 Notifications)		Death Rate per 1,000,000 p.a.	
	Male	Female	Male	Female	Male	Female
0–	11·9	12·2	0·60	0·89	70	110
1–4	15·7	17·8	0·06	0·05	9	9
5–14	5·2	6·0	0·005	0·01	0·3	0·9
15+	0·02	0·05	0·79	0·23	0·2	0·1

REFERENCE

1 *The Registrar General's Statistical Review of England and Wales for the Year 1956*, 1957, Part I, Tables, Medical. H.M.S.O., London.

Cervical Incompetence

Q.—*What are the recent advances in treatment of cervical incompetence causing repeated miscarriages, and what are the chances of success of operative treatment?*

A.—If cervical incompetence is present and other causes of repeated abortion have, so far as possible, been excluded, the results of operative treatment are good. Three groups of methods have been described. (1) Reducing the calibre of the whole cervical canal by an anterior longitudinal wedge resection.[1] (2) Producing a scar-ring at the level of the internal os by introducing talc granules subepithelially at that level.[2] These methods have in common that they are usually carried out when the patient is not pregnant, and they have the advantage that they do not necessitate caesarean section being required for delivery. (3) Encirclement of the cervix at the level of the internal os by a purse-string suture, usually subepithelially.[3–6] This operation may be performed either between pregnancies or during pregnancy; in the latter case some prefer to carry it out at the 14th to 18th week, while others wait till the 20th to 22nd week and will perform it as late as the 28th to 30th week. The ideal material for the suture is still being sought. Fascia (homologous and preserved), braided silk, nylon thread, and nylon tape have all been employed, while the use of kangaroo tendon and of synthetic "dacron" mesh are still being evaluated. The best method of eventual delivery is also a matter of opinion. When non-absorbable material has been used for the suture some prefer elective section, while others will cut the suture when labour starts and either remove it or reapproximate the ends after delivery.

The success of operative treatment in producing viable babies can be judged from the following reports. Lash and Lash[1]: 44 operations on non-pregnant women; 29 conceived, of whom 27 carried to term. Shirodkar[2]: 56 operations on non-pregnant women; 45 conceived and went to term. 43 operations on pregnant women; 34 were successful. McDonald[4]: Of his last 35 cases in pregnancy, 20 were successful. Green-Armytage and Browne[5]: 12 cases with 9 successes; the other 3 not yet pregnant. Barter[6]: 22 operations in pregnant women; 14 delivered successfully and 2 others not yet delivered but past the 30th week of pregnancy.

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5 Green-Armytage, V. B., and Browne, J. C. McL., *Brit. med. J.*, 1957, **2**, 128.
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Bachelor

Q.—*Why is the term "bachelor" used in association with academic degrees?*

A.—According to *Everyman's Encyclopaedia* and the *Concise Oxford Dictionary* this word is probably derived, through the old French *bacheler*, from the mediaeval Latin *baccalarius*, a word used in the 8th century to describe a farm servant (*baca*, Low Latin for *vacha*, a cow; cf. *vassal*). It was applied to a young knight who had no following of his own but fought under the banner of another (hence *knight bachelor*). Pope Gregory IX (1227–41) introduced the use of *baccalarius* to denote a person who had passed the first academical examination but was not yet a "master" or "doctor." The word was either corrupted or altered by a pun to *baccalaureus*, as if connected with *bacca lauri*, a laurel berry, from which we get the modern *baccalaureate*—university degree of bachelor. The English "bachelor" came to be used to describe an unmarried man who presumably still had to make his fortune.

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